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Annual Progress Report



♦ Fiscal Year 1991 ♦



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PE - Program Element	WU - Work Unit Accession No.

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**Headquarters
William Beaumont Army
Medical Center
El Paso, Texas 79920-5001**

**Annual Progress Report
Fiscal Year 1991**

**Clinical Investigation Program
RCS MED-300 (R1)**

**This report was prepared under the direction of
Colonel Manuel Schydlower
Chief, Department of Clinical Investigations
William Beaumont Army Medical Center
El Paso, Texas 79920-5001**

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FORWARD

During Fiscal Year 1991, the Department of Clinical Investigations (DCI) at WBAMC maintained an active and productive role in research and support of graduate medical education at our medical center (MEDCEN). Additionally, DCI responded to specific needs of Operation Desert Shield/Storm (ODS/S) at our facility by cross-training our civilian and military personnel in blood bank procedures to serve as backup for the anticipated mobilization of the blood bank. Of particular note, our Biological Research Service helped provide advanced trauma life support training to over 200 personnel mobilized to either augment the staff at our MEDCEN or deploy overseas in support of ODS/S.

DCI conducted a highly successful scientific awards research competition. Researchers at our MEDCEN submitted 24 entries involving papers published or accepted for publication and posters exhibited at meetings based on protocols approved by the hospital Institutional Review Board. Judging was principally done by faculty members of the Texas Tech School of Medicine Regional Academic Health Center in El Paso and awards were presented by DCI to several winners and finalists in clinical sciences, basic sciences, housestaff and health administration categories.

The clinical investigation activities involving DCI and the various departments of our MEDCEN progressed extremely well, reflecting a strong commitment to excellence and accomplishment in the field of research by our principal investigators. The numerous research initiative of several departments and the support provided by DCI were increasingly recognized not only as meritorious scientific endeavors, but also crucial for meeting residency review accreditation requirements.

In the past year, there were significant advances in the development of ongoing studies that relate to the health of AMEDD beneficiaries including active duty personnel and dependents. Among these were projects involving passive immunization of Klebsiella/Pseudomonas infection, tracheobronchial mucin in environmental exposure, prevention of stress fractures, Gortex graft tracheal reconstruction, intra/extra oral bone grafts, incisional wound strength, skin graft inhibition, Sickle cell trait human performance at simulated altitudes, measles immunity, youth risk taking/susceptibility to harm, perinatal drug abuse, and laser surgery training.

The accomplishments and successes of the past year were achieved thanks to the professionalism and dedication to excellence of the staff of DCI and principal investigators from all specialties at our MEDCEN. It is a privilege to be part of this accomplished team.

Manuel Schydlower, M.D.

MANUEL SCHYDLOWER
Colonel, Medical Corps
Chief, Department of Clinical Investigation

UNIT SUMMARY FY 91

Objectives

The Department of Clinical Investigation is responsible for providing the facilities and atmosphere of inquiry necessary to support and stimulate basic and clinical medical investigation within William Beaumont Army Medical Center.

Technical Approach

The Department of Clinical Investigation provides support for staff, fellows and housestaff research projects under the guidelines of the Clinical Investigation Program (AR 40-38); Use of Investigational Drugs in Humans and the Use of Schedule I Controlled Drug Substances (AR 40-7); Use of Volunteers as Subjects of Research (AR 70-25); Management of Clinical Investigation Protocols and Reports (HSC Reg 40-23); and The Use of Animals in DOD Programs (AR 70-18). Research protocols utilizing laboratory animals also adhere to the guidelines set forth in the "Guide for Laboratory Animal Facilities and Care" (published by the National Academy of Sciences-National Research Council) and the criteria established by the American Association for Accreditation of Laboratory Animal Care (AAALAC).

Research is conducted under protocols approved by the WBAMC Clinical Investigation Committee, Human Use Committee, Radioisotope Committee and Animal Use Committee, as applicable. Committee membership is governed by WBAMC Reg 15-1.

MANPOWER: Listed below is the strength of the Department of Clinical Investigation during FY 91.

<u>Description</u>	<u>Grade</u>	<u>M O S</u>	<u>Br</u>	<u>Req</u>	<u>Auth</u>	<u>Name</u>	<u>Rank</u>
C, Dept Cl Inv	06	60P	MC	1	1	Schydlower	06
Dir, HP/SCT	05	60F	MC	1	1	Weisman	05
Immunologist	03	68E	MS	1	1	Martig	05
Biochemist	03	68C	MS	1	1	Smith	03
C, Bio Res Svc	03	64C	VC	1	1	O'Hair	04
Animal Care NCO	E6	91T	NC	2	1	Williams	E5
Biol Sci NCO	E5	01H	NC	1	1	Fama	E6
Biol Sci Asst	E4	01H		1	1	Delgado	E4
Animal Care Sp	E4	91T		1	1	Kahn	E4
Animal Care Sp	E3	91T		2	1	Brown	E3
Supv Res Chem	12	1320	GS	1	1	Bhattacharyya	12
Microbiologist	12	403	GS	1	1	Veit	12
Chemist	09	1320	GS	1	1	Enriquez	09
Microbiologist	09	403	GS	1	1	Smiley	09
Med Technician	07	645	GS	2	1	Lund	07
Med Technician	07	645	GS	2	1	Mana	07
Med Technician	07	645	GS	2	1	McIntyre	07
Health Tech	07	640	GS	1	1	Revels	07
Cl Prot Coord	07	303	GS	1	1	Hineline	07
Edit Asst (Typ)	07	1087	GS	1	1	McCollum	07
Sup Clk (Typ)	05	2005	GS	1	1	Turner	04
Anm Caretaker	04	5048	WG	1	1	Sigholz	04
Anm Caretaker	01	5048	WG	2	1	Burton	01

Civilian Personnel with Special Project Funding

Co-Director HP/SCT				Zeballos
Research Nurse	11	610	GS	Chartrand
Exer Physiologist	09	413	GS	Connery
Health Technician	07	640	GS	Walker
Med Technician	06	645	GS	Badar
Edit Assistant	05	1087	GS	Peterson
Res Proj Clerk	04	303	GS	Morillo

PERSONNEL

	<u>Required</u>	<u>Authorized</u>	<u>Assigned</u>
Officers	7	5	5
Enlisted	7	5	5
Civilian	18	13	20*

* 7 civilians are funded through special projects

GRANTS:

USA Medical Research and Development Command

Prevention of Stress Fractures Through Modification of Basic Combat Training Physical Training Activities Based on Biodynamics. \$62,000

Intestinal Anastomosis with an Interpositional Absorbable Stent and a Neodymium (Nd):YAG Laser in the Rabbit Model \$15,020

Comparison of Cranial and Iliac Autologous Bone Grafts and Their Effect on the Success Rates of Subsequent Osseointegrated Intra/Extraoral Implant Application in the Miniature Swine. \$2,000

Tracheal Reconstruction with Synthetic Gore-Tex Grafts in the Rabbit Model. \$4,000

Efficacy of Passive Immunization in the Prevention of Infection due to Klebsiella pneumoniae and Pseudomonas aeruginosa \$50,700

Tracheobronchial Mucins in Health, Disease, and Toxic Exposures \$144,270

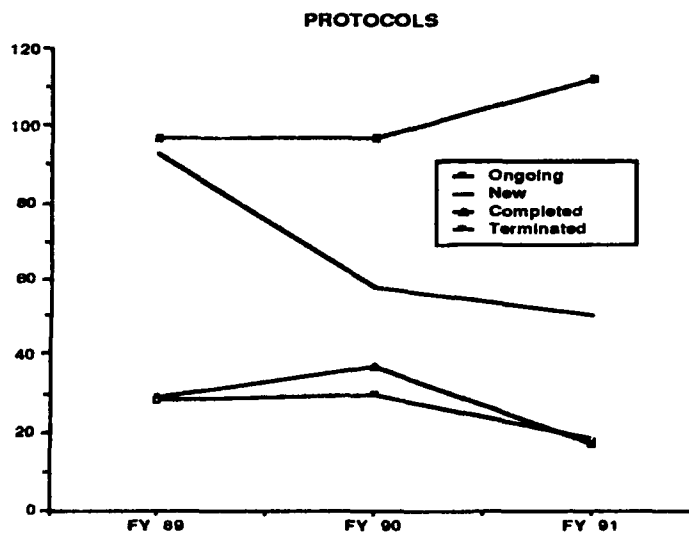
Effect of Fibrin Sealant on Skin Graft Inhibition of Wound Contraction in the Porcine Model \$1,300

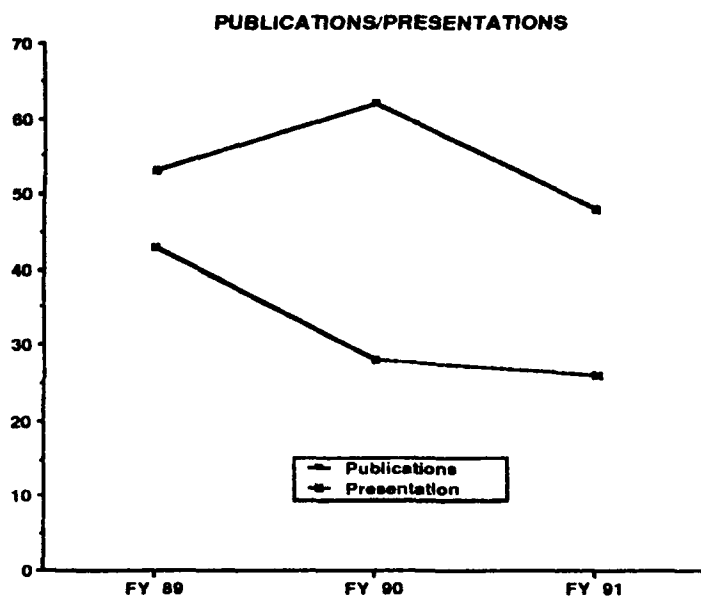
Effect of Fibrin Sealant on Breaking Strength of Incisional Wounds in the Porcine Model \$20,320

USN Medical Research and Development Command

Joint Navy-Army Human Performance/Sickle Cell Trait Research Project at WBAMC. \$88,951

PROTOCOLS, PRESENTATIONS, PUBLICATIONS:





EXPENDITURES	FY 89	FY90	FY91
Personnel (Civilian)	405,498	572,958	549,234
Consumable Supplies	187,846	221,572	233,612
Capital Equipment	23,835	91,748	46,884
TDY	4,605	6,128	8,030
Printing and Publications	<u>4,103</u>	<u>3,019</u>	<u>2,886</u>
TOTAL	625,887	895,425	840,646
MEDCASE Equipment	361,427	62,116	58,000
Military Pay	<u>510,814</u>	<u>538,711</u>	<u>536,758</u>
TOTAL	1,498,128	1,496,252	1,435,404

PROGRESS FY 91

Biological Research Service

The Biological Research Facility is fully accredited by the American Association for the Accreditation of Laboratory Animal Care (AAALAC). The outcome of the most recent AAALAC inspection in June 1990 was reported during this FY and affirmed full accreditation and several noteworthy aspects of the program. The facility totals 6,984 sq ft and during FY91 had an average daily inventory of 165 animals.

The facility has continued to support the total animal research and training mission for William Beaumont Army Medical Center and other regional MEDDACs. The biomedical training utilizing animal models is primarily for the physician resident training programs. There are 15 ongoing training protocols for physicians encompassing emergency trauma life support, general surgery, laser surgery, laparoscopic surgery, and microsurgery. In addition, there are two protocols for training field medics and paramedics in emergency trauma life support procedures. There are a total of 13 active research protocols involving: microsurgery, general surgery, soft tissue and orthopedic reconstructive surgical techniques, laser surgery for visceral repair, pathophysiology of orthopedic stress, therapeutic efficacy, molecular biology, and immunology.

The Department of Surgery collaborated with the Biological Research Service to provide early and ongoing support of Operation Desert Shield in the form of Advanced Trauma Life Support (ATLS) training for deploying personnel, both from Ft Bliss and from other facilities. This collaborative support continued as more medical personnel arrived and were deployed.

The Biological Research Service initiated a collaborative training agreement with Sierra Medical Center during the FY involving at least seven surgical and medical disciplines with emphasis on advanced laser, laparoscopic and endoscopic techniques. Approximately 17 WBAMC physicians were certified in specific subspecialties during this collaboration at a greatly reduced cost to the government.

Significant acquisitions of equipment were added to the Service's inventory during the FY which enhanced training and research support. Included is a laparoscopic surgical system which has enabled routine in-house laparoscopic training for OB/GYN and general surgery staff.

Chemistry Section

The Chemistry Section of DCI is involved with research projects concerning gene regulation of mucin production in respiratory diseases, the role of vitamin B₆ in human health and diseases and analysis of drug metabolites in children of addicted parents. Rat and rabbit tracheal epithelial cells have been propagated successfully on collagen-coated dishes containing serum-free and hormone-supplemented medium. The presence of retinoic acid and EGF in the medium is essential for the normal growth as well as production of mucin in these cell lines, indicating that these components are partially responsible for the expression of mucin gene in these systems. Different respiratory drugs and chemical reagents, including carcinogens,

have also been found to affect the production of mucin in these cell lines. Total RNA and mRNA have been isolated from these cells and found to hybridize with a mucin-related DNA probe. We are now systematically studying the expression of the mucin gene in these cells that are grown in presence of the reagents cited above. The purchase of an environmental chamber system for toxic inhalent exposure is underway. As soon as the system is established, the effects of different toxic substances, such as NO₂, SO₂ etc., on the production of mucin in rat trachea will be studied. This study has been funded by a grant from USAMRDC.

Vitamin B6 studies continue in two main areas. First, research is being done on the effect of L-asparaginase on plasma vitamin B6 levels and amino acid profiles, with and without B6 supplementation in the rabbit model. The other area of vitamin B6 research involvement is a co-operative effort with Dr. William Becker of the Army Institute of Surgical Research at Ft. Sam Houston, involving the correlation of plasma vitamin B6 levels with trauma in burn victims.

Another ongoing protocol, concerning the determination of the prevalence of drug affected babies in the military population, has been expanded into a co-operative protocol with the TexasTech University School of Medicine to also include a look at the civilian population. This protocol will involve not only thin layer chromatography drug screens, but also complicated gas chromatography/mass spectrometry and liquid chromatography/mass spectrometry techniques.

Molecular Biology Service

The Department of Clinical Investigation has a newly formed Molecular Biology Service that has the laboratory facilities and technical expertise to perform studies involving the evolving recombinant DNA technologies, to include:

- Construction of 'libraries' of DNA from cells or tissue in a variety of vectors and host strains.
- Isolation of genes with the use of molecular probes of DNA, RNA or antibodies by use of the proper vectors.
- Characterization of coding regions of genes as well as the respective control regions by direct sequence determination and by functional studies.

Current projects include a study concerned with genetic control and is in conjunction with the Chemistry Section of DCI. The project is designed to determine the processes of mucin gene expression and the involvement of regulatory mechanisms in secretory dysfunction as manifested in disease. A second area of investigation, involving several projects, is ongoing with investigators in the Departments of Pathology, OB/GYN, and Adolescent Medicine. These protocols utilize molecular techniques for identification of pathologically important strains of Human Papillomavirus in a variety of patients. For a related study, an inter-institutional collaboration between Texas Tech School of Medicine, the University of Texas-El Paso School of Nursing and our Molecular Biology Service has been established for the study of the prevalence of Human Papillomavirus within the indigent Hispanic population of El Paso.

Immunology and Microbiology Section

Present research interests of the Immunology and Microbiology Section are focused on (1) immunoregulatory subsets of T cells in Bermuda grass allergy, (2) epidermal growth factor production in peptic ulcer disease and colon malignancy, and (3) immune responses to measles virus. In addition, our section is currently developing a new research program to study growth factors, tumor-associated antigens, cellular infiltrates, and overall growth dynamics which influence the survival and outgrowth of chemically resistant human breast cancer cells.

It has been hypothesized that suppressor T cells develop as one consequence of immunotherapy and that these suppressor cells are responsible, at least in part, for the amelioration of symptoms in allergy patients who undergo immunotherapy. We have attempted to detect a subset of suppressor T cells in the blood of patients with Bermuda grass allergy who were undergoing immunotherapy. By utilizing a protocol that had been reported to demonstrate the existence of such a population in patients with ragweed allergy, we were able to confirm those findings in our study group but were unable to demonstrate suppressor cell activity in Bermuda grass allergy patients. It was concluded that the quality and/or quantity of antigen used, as well as the cellular composition of the population stimulated in vitro, are critical factors in the generation of suppressor cells.

Epidermal growth factor (EGF) is a member of a large family of growth-promoting factors that are required for tissue repair and cell growth following tissue damage due to injury or disease, including cancer. EGF may play a significant role in promoting peptic ulcer disease. Normally, EGF is an inhibitor of the production and secretion of gastric acid. However, patients with peptic ulcer disease may have reduced levels of EGF production which may be one of the contributing events in the development of their disease. We have established a sensitive radioimmunoassay and, more recently, an ELISA assay for measuring picogram quantities of EGF in our laboratory. Results thus far have shown that all patients with peptic ulcer disease tested have reduced levels of salivary EGF. Currently, we have extended our studies to the survey of sera from patients with colon carcinomas to determine whether EGF levels are indicative of disease progression.

In the past few years, there has been serious concern among communicable disease personnel regarding the high incidence of measles epidemics in the United States. Recent outbreaks in El Paso have provided the opportunity to study military dependent populations of students who received immunizations during the epidemics as well as infant and adult patients who are admitted to the hospital with primary measles disease. We have established an ELISA to measure total IgG, IgG subclasses, IgA and IgM antibodies to the measles virus. Our studies of pre- and post-immunization sera from these children have indicated that approximately 9 to 10% of previously-vaccinated adolescents have very little, if any, durable immunity to measles since, upon revaccination, they experience a four-fold or greater increase in their IgG titers. Whether these individuals are at risk of developing clinical disease upon exposure to wild-type virus is uncertain. However, it is believed that waning or non-durable immunity may be one explanation for the increased incidence of measles outbreaks. We are currently testing the same sera for pre- and post-vaccination levels of anti-rubella antibodies to determine whether the same 10% are also deficient in rubella immunity as well.

RESEARCH AWARDS COMPETITION

The Department of Clinical Investigation conducted a highly successful Scientific Awards Research Competition. Entries submitted by WBAMC researchers involved papers published or accepted for publication and posters exhibited at meetings based on protocols approved by the WBAMC Institutional Review Board (IRB).

Judging of entries was accomplished by faculty members of the Texas Tech University School of Medicine Regional Academic Health Center in El Paso. Results are listed below.

Clinical Sciences

1st Place: LTC Idelle M. Weisman, MD, Department of Clinical Investigation
Reliability of Non-invasive Oximetry in Black Subjects during Exercise and Hypoxia

Finalists: MAJ David M. Maccini, MD, Department of Medicine
The Yield of Barium Enema in Patients Undergoing Inguinal Hernia Repair or Abdominal Hysterectomy

Bruce C. Veit, Ph.D., Department of Clinical Investigation
Serological Response to Measles in a Highly Immunized Military Dependent Adolescent Population

Basic Sciences

1st Place: MAJ David M. Maccini, MD, Department of Medicine
Salivary Epidermal Growth Factor in Patients with and without Acid Peptic Disease

Finalists: COL David L. Michaels, MD, Department of Medicine
In Vitro Qualitative ELISA Testing as a Screening Tool for Significant Allergy

S. N. Bhattacharyya, Ph.D., Department of Clinical Investigation
Neutral and Acidic Human Tracheobronchial Mucin

Housestaff

- 1st Place:** CPT Jay Carlson, MD, Department of Obstetrics & Gynecology
Evaluation and Treatment of Human Papillomavirus Infection in Men
- Finalists:** CPT M. Mitchell Silver, MD, Department of Obstetrics & Gynecology
Comparison of Two Endometrial Biopsy Instruments: Novak's vs Pipelle
- CPT Connie R. Butterfield, MD, Department of Obstetrics & Gynecology
Routine Screening for Hepatitis B in an Obstetric Population

Administrative

- 1st Place:** CPT Kim C. Strunz, Military Personnel Division
Employee Surveys as a Strategic Management Tool: The Case of Army
Physician Retention
- Finalists:** MAJ Henry Hernandez, MS, Clinical Support Division
A Study to Assess the Training Needs of William Beaumont Army Medical
Center Staff and to Determine a Strategic Plan for Transition to Diagnosis
Groups
- MAJ Peter Moskowitz, MS, Clinical Support Division
A Psychosocial View of Health Care in the Army

Scientific Poster

- 1st Place:** R. Jorge Zeballos, MD, Department of Clinical Investigation
Validation of Gas Exchange Measurements above the Anaerobic Threshold
during Incremental Exercise
- Finalists:** Rebecca Smiley, Department of Clinical Investigation
Two-Color Immunofluorescence Analysis of IL-2R Expression on T Cell
Subsets in Peripheral Blood of Bermuda Grass Allergy Patients
- MAJ Elisabeth M. Stafford, MD, Department of Pediatrics
Echocardiographic Changes during Pubertal Maturation: Analysis by Sex
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Leventhal EK: Xanthogranulomatous pyelonephritis involving the pancreas. Surg, Gynecol and Obstet, 21 May 1991.

Reyna TM: Familial Hirschsprung's: Study of a Texas Cohort. Southwestern Surgical Congress, 1991.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 86/17

STATUS: Ongoing

TITLE: Human Tracheal Mucin: Biochemical, Physical and Rheological Studies

START DATE: Mar 86

ESTIMATED COMPLETION DATE: Oct 92

PRINCIPAL INVESTIGATOR: Sam Bhattacharyya PhD

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Brigitta Manna, John I. Enriquez

KEY WORDS: Tracheal mucin, Human

Study Objective: This protocol is concerned with isolation, purification and characterization of mucin glycoprotein components (mucins) from tracheal secretion of patients with asthma, chronic bronchitis and cystic fibrosis. The glycosylated and nonglycosylated peptides will be isolated, purified and sequenced (peptide portion) after subjecting the purified mucins with different proteolytic enzymes. Antibodies will be developed in rabbits against the nonglycosylated peptides which, in turn, will be used to follow the synthesis and secretion of these macromolecules in a tracheal (or bronchial) culture system. Finally, the viscoelastic properties of purified mucins will be investigated.

Technical Approach:

1. Collect sputum from patients (either male or female, any age) with asthma, chronic bronchitis and cystic fibrosis.
 2. Solubilize mucins with water and buffer.
 3. Establish the homogeneity of mucin glycoproteins isolated from sputum of patients with asthma, chronic bronchitis, and cystic fibrosis by molecular sieve and ion-exchange chromatography.
 4. Isolation and characterization of peptides (or glycopeptides) derived from digestion of mucins with different proteolytic enzymes (Column and HPLC);
 5. Amino acid sequence analysis of these peptides by sequenator and cDNA cloning procedure;
 6. Raise antibodies in rabbits against these peptides (preferably against nonglycosylated peptides); and finally,
 7. Establish a tracheal (or bronchial) culture system to examine the synthesis and control in secretion of these macromolecules by ELISA or radioimmunoassay (RIA) procedures using these antibodies.
- In addition to the above, the physical properties of mucins, particularly their interaction (in terms of viscosity) with other serum proteins (such as albumin, immunoglobulin, and fibronectin) will be studied.

Progress: Work is in progress to isolate a sufficient quantity of the major peptide component (P_1) of the deglycosylated human bronchial mucin by high pressure liquid chromatography. This peptide will be utilized to raise monoclonal antibody in mouse. The antibody will, in turn, be utilized to detect the translation product made by mucin mRNA isolated from lungs of different animals. In addition, this antibody will be used to screen human mucin cDNA library.

Reference: Bhattacharyya SN; Velt BC; Manna B; Enriquez JI; Walker MP; Khorrami AM; and Kaufman B: Neutral and acidic human tracheobronchial mucin. *Inflammation* 14: 355-373 (1990).

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/16

STATUS: Ongoing

TITLE: Cellular Mechanism of Mucin Secretion: Studies Involving Rat and Rabbit Tracheal Culture System

START DATE: Jan 89

ESTIMATED COMPLETION DATE: Oct 92

PRINCIPAL INVESTIGATOR: Sam Bhattacharyya PhD

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Brigitta Manna, Maxine Lund, John I. Enriquez

KEY WORDS: Mucin, animal

Study Objective: This proposal is concerned with the isolation and characterization of mucin glycoprotein components (mucin) from secretions of rat and rabbit tracheal epithelial cells in culture and establishing their structural identity with those of the same components from human. The ultimate goal of this proposal is to find an animal model tracheal culture system akin to human where the control mechanism of the secretion of mucins can be studied on the gene level.

Amendment August 1989: In addition to isolation of mucin proteins in the rat and rabbit models, it has become apparent that the isolation and characterization of mucin glycoprotein components from secretions of porcine (swine) tracheal epithelial cells in culture is also necessary. Once the mucin fraction is characterized at the structural level, it can be determined if it is comparable with the same components of human tracheal mucin. The ultimate goal of this proposal is to find an animal model tracheal culture system akin to human where the control mechanism of the secretion of mucins can be studied on the gene level.

Technical Approach: Growth of epithelial cells from rat and rabbit bronchial tissues: Rats and rabbits will be euthanatized and normal appearing tracheal tissues excised aseptically, immersed in cold, sterile L-15 culture medium containing penicillin/streptomycin and transported on ice to the laboratory. Lung tissue is sterilely trimmed away and the bronchus cut into large fragments. Cells are isolated from the human bronchus after an overnight incubation with 0.1% protease solution in minimal essential medium (MEM, Ca++ free) done at 4 degrees C. The next day, incubated bronchi are flushed with MEM plus 10% Fetal Calf Serum to remove the digested cells. The cells are washed several times to remove any protease, which is toxic to epithelial cultures. The cell suspension is filtered through a sterile 100U nitrex filter and centrifuged for 10 minutes. Cell pellets are resuspended in cold MEM with 10% FCS and centrifuged again. The cold protease overnight treatment is sufficient to remove most epithelial cells lining the bronchus without much contamination of other cell types from the layer under the basement membrane. After the total cell count is taken, primary cultures are normally initiated by plating $1-2 \times 10^6$ cells per ml per 35mm culture dish. The culture conditions are used for the human bronchial epithelial cells consist of M199 media with D-valine substituted for D1-valine, 10% Fetal Calf Serum, L-glutamine, penicillin/streptomycin, gentamicin, insulin, transferrin, epidermal growth factor, hydrocortisone, cholera toxin, bovine hypothalamus extract, and fungizone. Primary epithelial cultures were then placed in an incubator, with conditions of 37 degrees C., 5% CO₂, and 95% air, and cells allowed to adhere to the culture dish. After 3-4 days incubation, a confluent primary culture of epithelial cells is routinely observed. The cultures received media change and can be used in various studies.

Secretion of mucin and characterization: The synthesis of mucin will be followed by ³H glucosamine and ³⁵SO₄ incorporation. Once the saturation curve is established, radioactive agents will not be used anymore. At the time of maximum secretion, the culture medium will be collected, lyophilized and chromatographed on Sepharose 2B and ECTEOA column. The purified mucin will be deglycosylated by chemical procedure and the peptide portion will be partially sequenced by sequenator.

Isolation of mucin mRNA and sequencing by cDNA method: The procedure that will follow here is essentially that of Timppte et al. mRNA from tracheal culture will be isolated by guanidine isothiocyanate method followed by oligo(dt)-cellulose chromatography. Construction and screening of the cDNA library utilizing human antilapomucin will be done as described.

Control in secretion of mucin: The synthesis of mucin in epithelial culture will be followed by ³H glucosamine and ³⁵SO₄ incorporation. The control in synthesis will be studies on transcriptional and translational levels using different inhibitory (acetylcysteine and cyclohexamide) and enhancing (pilocarpine) reagents.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Animal usage: 66 rabbits; 288 rats and 1 swine. Rabbit tracheal epithelial cells, cultured on collagen-coated dishes in serum-free and hormone-supplemented medium, have been found to secrete high molecular weight components in medium. The secreted material was digested with hyaluronidase and the components were purified by sepharose 2B column chromatography. The chemical analyses of these products resulted in a profile which resembled that of mucous glycoproteins (mucins). The incorporation of [³H] glucosamine into mucins was inhibited by three aryl-N-acetyl-galactosamimides and a chemical carcinogen, N-nitroso-N-ethyl urea, whereas 5-azacytidine enhanced the proliferation of cells as well as the radiolabeling of mucins. Parasympathetic agent (pilocarpine), cholinergic antagonist (atropine) and β -adrenergic agonist (isoproterenol) alone have little effect on the secretion of mucins. Transmission electron microscopy exhibited mucus-secreting granules in some of the control cells, but not in the cells treated with chemical reagents (see reference). Attempts are now being made to culture rat tracheal epithelial cells and study the mucin gene expression in these cells.

Reference: Bhattacharyya, SN; Ashbaugh, P; and Manna, B: Biosynthesis of mucins by rabbit tracheal epithelial cells in culture. Communicated to Inflammation (1990).

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/37

STATUS: Ongoing

TITLE: Tracheobronchial Mucins in Health, Disease, and Toxic Exposures

START DATE: Oct 90

ESTIMATED COMPLETION DATE: Oct 92

PRINCIPAL INVESTIGATOR: Sam Bhattacharyya PhD

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Bruce C. Velt, PhD, CPT David J. Smith, PhD

KEY WORDS: Bronchial mucin

Study Objective: This proposal has two objectives. One is to prepare a library of mouse monoclonal antibodies against human and rat lung mucin apoprotein to be used as probes for the study of structure and biosynthetic regulation of mucin in tracheal epithelial culture system both at the cellular and DNA level. The other objective is to study the levels and control of transcription and mucin in RNA accumulation in rat tracheal epithelial cells in cultures in response to various noxious agents, like tobacco smoke, ammonia, SO₂, and NO₂, and different drugs.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Animal usage: 454 rats and 80 mice. The major studies in this project are already in progress. The main purified peptide component (P₁) of human bronchial mucin has been purified and is now being utilized to produce monoclonal antibody in mouse. Attempts to identify and estimate the mucin mRNA from pig and rat are being made now with some success. Rat tracheal epithelial culture system has been successfully propagated on collagen-coated dishes in serum-free and hormone-supplemented medium. Different respiratory drugs on the production of mucin have already been tested in this culture system and the results are satisfactory.

This project has been funded for two years by MRDC. Work is in progress now to acquire a toxicology chamber and suitable housing for this chamber. As soon as this facility is built, the research work on mucin gene expression in rats exposed to different toxic substances will begin.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 86/28

STATUS: Completed

TITLE: Measurement of Plasma Pyridoxal 5'-Phosphate in Seriously Ill Patients and Effect of Supplementation of Pyridoxine HCL on Laboratory Tests (Monitor: COL Stephenson)

START DATE: Mar 86

ESTIMATED COMPLETION DATE: Feb 92

PRINCIPAL INVESTIGATOR: John Enriquez

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Stephen Carey, MC, PFC Ismael Delgado

KEY WORDS: PLP

Study Objective: Gather evidence of vitamin B6 deficiency in hospitalized patients and determine if plasma pyridoxal 5' phosphate levels can be restored easily to normal. Determine effect of PLP level changes on other measured parameters.

Technical Approach: All surgical patients will have a plasma PLP, CBC and SMAC-20 drawn on admission or, in the case of elective surgeries, as part of the pre-admission lab work. Those patients found to have a plasma PLP of greater than 20 nM will not be entered into either the B₆S or the NS group. If the initial or subsequent plasma PLP goes below 20 nM, the patient will be assigned the B6S or NS group on the basis of the last digit of their social security number. He will be given 50 mg/day or 0 mg/day of PN:HCl if his plasma PLP is between 10 and 20nM, and 100 mg/day or 50 mg/day of PN:HCl if his plasma PLP is less than 10 nM. After one week of no supplementation (for those in the NS group) or one week of supplementation (for those in the B6S group), a repeat plasma PLP, CBC and SMAC-20 will be drawn. Whenever the plasma PLP exceeds 20 nM, supplementation with PN:HCl will stop and further plasma PLP levels will be drawn weekly and at pre-discharge.

Progress: Projected completed, data analyzed and reported.

Conclusion: The measurement of PLP in seriously ill patients and the effect of B6 supplementation yielded a great deal of information as to the role of Vitamin B₆ in the patient's treatment and healing phases. Vitamin B₆ appears to be an important factor in regards to the state of "wellness" of a patient. By this, we mean that we found a direct correlation between a patient's level of health and plasma PLP levels. B₆ was also found to be a significant parameter when dealing with the use of aminoglycoside antibiotics and other medications which were found to be B₆ antagonists. Vitamin B₆ also aided in avoiding some of the adverse effects of these medications.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/13

STATUS: Ongoing

TITLE: The Effect of L-asparaginase on Pyridoxal-5'-Phosphate Levels in the Rabbit Model

START DATE: Apr 90

ESTIMATED COMPLETION DATE: Dec 91

PRINCIPAL INVESTIGATOR: John I. Enriquez

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Stephen R. Stephenson (MAMC), COL Michael Weir (MAMC)

KEY WORDS: L-asparaginase, Pyridoxal-5'-Phosphate

Study Objective: The objective of this study is to test whether L-asparaginase has an effect on serum pyridoxal-5'-phosphate levels.

Technical Procedure: Following a period of quarantine and observation, the rabbits will be brought to the operating suite in groups of six. Each group of six rabbits will be treated in the following manner:

Rabbit #1, rabbit #2, rabbit #3: 100 u/kg IM L-asparaginase + 10 mg pyridoxine 15 to 30 minutes apart.

Rabbit #4, rabbit #5, rabbit #6: 100 u/kg IM L-asparaginase + saline 15 to 30 minutes apart.

These medications will be repeated daily for five days. On days 1, 3 and 5, blood will be drawn twice from an ear vein for PLP, asparagine, glutamine, albumin and total protein. Blood will be drawn: one (1) hour before and two (2) hours after medication administration. Blood, for the same analyses, will also be drawn once on day 8 of the following week. Following the last injection and blood draw the rabbits will be returned to the control of the BioResearch Service. In each of two subsequent weeks, six more rabbits per week will be studied similarly. This is a detailed study that hopes to show that there is a specific relationship between the administration of L-asparaginase and the average fall in PLP as well as the asparagine, glutamine, albumin and total protein levels.

Amendment:

a. Experimental Design: Following a period of quarantine and observation, the rabbits will be brought to the treatment room in blocks consisting of a minimum of 4 rabbits (one rabbit per experimental group). Each block of rabbits will be treated in the following manner:

Group A rabbit(s): 100 IU/kg L-asparaginase + 10mg pyridoxine 15 to 30 minutes apart IM.

Group B rabbit(s): 100 IU/kg L-asparaginase + 0.1ml saline 15 to 30 minutes apart IM.

Group C rabbit(s): 10mg pyridoxine + 0.1ml saline 15 to 30 minutes apart IM.

Group D rabbit(s): 0.1ml saline + 0.1ml saline 15 to 30 minutes apart IM.

These medications will be repeated daily for five days. On days 1, 3, and 5, blood will be drawn twice from an ear vein for PLP, asparagine, glutamine, albumin, total protein, BUN and creatinine. Blood will be drawn one hour before and two hours after medication administration. Blood for the same analyses will also be drawn once on day 8. Following the last blood draw, the rabbits will be returned to the control of the Biological Research Service. In each of the subsequent weeks, a minimum of one block of rabbits per week will be studied similarly until either enough statistical data is obtained or a total of thirty-six (36) rabbits are utilized. This is a detailed study to attempt to show there is a specific relationship between the administration of L-asparaginase and the average fall in PLP as well as changes in the asparagine, glutamine, albumin, total

protein, BUN and creatinine levels.

c. **Determination of Number of Animals Required:** Thirty-six (36) rabbits will be used. Based upon similar studies, it was determined that 9 animals per group is the minimum number required to generate statistically valid data.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Animal usage: 20 rabbits. Mr. Enriquez assumed PI responsibility due to COL Stephenson's PCS to MAMC in Jun. Twenty animals have been treated. In order to complete the project, 16 more rabbits need to be treated. Sixteen sets of samples have been analyzed for Vitamin B₆ (plasma), SMAC 20 and amino acid levels. Four more sets have been received and are currently being analyzed. To date, the data appears to show that use of L-asparaginase does affect the amino acid balance and that, with B₆ supplementation, this balance remains undisturbed.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/14

STATUS: Ongoing

TITLE: Protective Role of Pyridoxine in Gentamicin Nephrotoxicity (in the Rabbit Model)

START DATE: Apr 90

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: COL Manuel Schydlower

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Mohammed A. Nadjem, MC; John I. Enriquez, Sr.; COL Michael Weir, MC

KEY WORDS: Pyridoxine, Gentamycin, Nephrotoxicity

Study Objective: The objective of this study is to test whether pyridoxine has a protective effect on gentamicin nephrotoxicity.

Technical Approach: Following a period of quarantine and observation, the rabbits will be brought to the operating suite in groups of seven. Each group of seven rabbits will be treated in the following manner:

- rabbit #1 - 100 mg pyridoxine (control)
- rabbit #2 - 10 mg/kg gentamicin (IM), 10 mg pyridoxine
- rabbit #3 - 10 mg/kg gentamicin (IM), 100 mg pyridoxine
- rabbit #4 - 10 mg/kg gentamicin (IM), saline
- rabbit #5 - 40 mg/kg gentamicin (IM), 10 mg pyridoxine
- rabbit #6 - 40 mg/kg gentamicin (IM), 100 mg pyridoxine
- rabbit #7 - 40 mg/kg gentamicin (IM), saline

These medications will be repeated every morning for five days. Blood will be drawn from an ear site for PLP, gentamicin and creatinine on days 0, (before injections begin), and two hours after injection on days 1, 3 and 5. Following the last injection and blood draw in the morning, the rabbits will be euthanized in the early afternoon and one kidney from each animal will be recovered for fixation for blinded pathologic interpretation.

In each of two subsequent weeks, seven more rabbits per week will be studied similarly. This is a descriptive study that hopes to show that there is a general relationship between the renal pathology and the average fall in PLP, and/or there may be a relationship between pathology and gentamicin blood levels.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in Item 5.b. (Animal Procedures).

Progress: Therapeutic use of gentamicin (GM) in a clinical setting may result in nephrotoxicity, most commonly presenting as acute tubular necrosis (ATN). We have previously observed decreased plasma pyridoxal 5'-phosphate (PLP) levels in rabbits given therapeutic doses of GM and endeavored in this study to determine if vitamin B₆ supplementation (B₆S) could protect against the nephrotoxicity of GM. Twenty-one rabbits were randomly assigned to one of seven treatment groups of three rabbits each. Three of the groups received GM 10mg/kg with either 10mg B₆S, 100mg B₆S, or 0.9% saline. Three of the groups received GM 40mg/kg with either 10mg B₆S, 100mg B₆S, or normal saline. The control group only received 100mg B₆S. All treatment were administered by intramuscular route once daily for five days. Blood was drawn for chemical assays on day zero (prior to any treatments) and two hours after each respective treatment on days 1, 3, and 5. After five days, the rabbits were euthanatized and kidneys were excised for histological evaluation by light microscopy. At the 40mg/kg/d of GM, significant mild to moderate ATN was observed in the saline controls,

which was prevented by either dose of B₆S. Only a few animals given 10mg/kg/d of GM showed any renal pathology and that was minimal. Unexpectedly, one rabbit given only 100mg/d of B₆S, but no GM, showed interstitial nephritis with focal ATN. We conclude that vitamin B₆ can protect against the nephrotoxicity of GM in rabbits, but that further study is needed on the possible nephrotoxicity of high doses of B₆S. Paper being considered for publication.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/42

STATUS: Ongoing

TITLE: Risk for Accidental Hot Tap Water Burns

START DATE: Jul 91

ESTIMATED COMPLETION DATE: Jan 92

PRINCIPAL INVESTIGATOR: COL Manuel Schydlower

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Bruce Pichoff (TAMC), COL Stephen R. Stephenson (MAMC)

KEY WORDS: Accidental burns, Hot Water

Study Objective: To identify the risk for hot tap water (HTW) injury and assess knowledge about safety limits at our military installation family housing area.

Technical Approach: Sixty family housing units were selected at random for measurement of HTW temperature using both an electronic thermometer and a mechanical thermometer (Oct 88-Mar 89). Household members were asked about their knowledge of HTW safety limits and their awareness of the risk for HTW injury. This study will integrate the epidemiological, retrospective, and descriptive review of the collected data into a final paper.

Progress: The American Academy of Pediatrics identifies young children at risk for accidental HTW burns and recommends that HTW temperature be set no higher than 49°C (120°F). Studies report that a temperature of 52°C (125°F) can cause a full thickness burn in two minutes, and a temperature of 54°C (130°F) can result in a full thickness skin burn in thirty seconds. The above study of 60 randomly selected family housing units at Fort Bliss identified 53 (88%) with HTW temperatures greater than 52°C (125°F) including 44 (73% with HTW temperatures greater than 54°C (130°F). At the time of this study in 1988, existing post guidelines specified that HTW temperature be set at 60°C (140°F) or less, which was arbitrarily accomplished by setting hot water heaters at the medium setting. The range of the medium setting was found to be from a low of 43°C (110°F) to a high of 43°C (110°F). There were temperatures that were unsafe at all heater settings. As a result of this study, personnel in housing, engineering and mechanical branches at Fort Bliss developed and implemented safety measures that included setting maximum HTW temperatures in housing units no higher than 49°C (120°F), periodic checks (twice a year), and new post guidelines to ensure safe HTW temperature limits (USAADCENFB Reg 11-27, 15 Aug 90). Final paper in preparation.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/46

STATUS: Ongoing

TITLE: Adolescent Health Care in the Army Medical System

START DATE: Jul 91

ESTIMATED COMPLETION DATE: Jan 92

PRINCIPAL INVESTIGATOR: COL Manuel Schydlower

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Walter Imai

KEY WORDS: Adolescent, Health Care, Military Dependents

Study Objective: To define the primary care needs of the adolescent dependent patient and to examine the care available and needed for this population in the AMEDD system.

Technical Approach: Epidemiologic, retrospective, data on care availability reported by health care facilities in the AMEDD and clinical diagnoses along with demographic data collected by a single provider over a 2-year period will be integrated into a final descriptive paper. Data includes upper age limit for pediatric care, principal diagnoses, patient age and sex, provider specialty, separateness of care facility, consent requirements for care, and chaperonage. Data are not traceable to any individual patient. Data about care availability are not traceable to a particular AMEDD facility. Information derived from the data is described and not compared.

Progress: Overall, MEDDAC pediatric practices offered much less general, gynecologic, counseling, sports medicine, and inpatient care to adolescents than did MEDCEN pediatrics and all family practice groups. All MEDCEN pediatric departments offer essentially all appropriate services to all adolescent patients seeking care. More than half of the adolescent population is ineligible for pediatric care at most MEDDACs. The older adolescent, in particular, is shunted to a variety of acute care providers, including non-physician extenders. Inadequate staff levels necessitate limiting care by many pediatric services at the community hospital level, resulting in underserving of the adolescent patient. An average requirement of two additional physicians per MEDDAC was projected in order to fully serve the eligible population. Final paper is in preparation and will include demographics and diagnostic categories of 3439 visits to WBAMC Adolescent Clinic.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 88/04

STATUS: Ongoing

TITLE: Activation of T-Cell Subsets in Bermuda Grass Allergy Patients

START DATE: Nov 87

ESTIMATED COMPLETION DATE: Aug 92

PRINCIPAL INVESTIGATOR: Bruce C. Veit PhD

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Stanislaus Ting, MD; LTC RV Charya, MC; Rebecca Smiley, BS; Susan McIntyre

KEY WORDS: Allergy, T-cells subsets, Immunoregulation

Study Objective: To determine whether there are detectable changes in numbers and functions of manifestations of Bermuda grass allergy. Since T4+ cells are associated with helper/inducer functions and T8+ cells are associated with cytotoxic/suppressor functions, alterations in the numbers of T4+ or T8+ activated T cells may correlate with changes in the immunoregulatory processes involved in controlling the allergic state. Peripheral blood samples will be obtained from patients during active allergy, immunotherapy, and disease quiescence. Samples will be analyzed by 2-color flow cytometry and by immunohistochemical staining for the distribution of T4+ and T8+ cells and the percentage of activation antigen-positive cells within each of these subsets. T cell subsets will also be analyzed for their ability to increase or suppress the synthesis and/or secretion of IgE. Serum samples from these patients will be analyzed for the presence of soluble IL-2R (circulating IL-2 receptor). These studies should improve our understanding of the immunoregulatory processes involved in the control of IgE-mediated allergic responses.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: The study has focused on the immunological responsiveness of peripheral blood lymphocytes (PBL) from Bermuda grass allergy patients (BGA-PTS) and long-term (>2 years) BGA-immunotherapy patients (IT-PTS). As previously reported, cells from IT-PTS were found to be unresponsive to BGA but significantly responsive to an unrelated allergen, Mulberry pollen allergen (MPA), whereas cells from BGA-PTS were highly responsive to both allergens. Cells from BGA-PTS exhibited a significantly higher level of activation than did those from IT-PTS suggesting that immunotherapy had reduced the allergenic response. Serum levels of BGA-specific IgG and IgE antibodies correlated with symptoms and levels of lymphocyte activation, i.e., BGA-PTS exhibited higher levels of IgE and lower levels of IgG relative to IT-PTS who exhibited higher levels of IgG and lower levels of IgE confirming the efficacy of immunotherapy.

Our results suggest the possibility that immunotherapy may enhance the development of suppressor cells which effect the observed hyporesponsiveness of cells from ITS-PTS. In an attempt to demonstrate the putative suppressor cell population *in vitro*, we utilized an approach that was used by others to demonstrate the presence of suppressor cells in ragweed allergy patients. For comparison, cells from short-term immunotherapy patients (who had allergies to both Bermuda grass and ragweed) were tested for the presence of suppressor cell activity. Results showed that approximately one-third of these patients had demonstrable suppressor cell activity that was directed toward ragweed allergy and confirm those previously reported. However, none of these patients had detectable suppressor cell activity that was directed toward Bermuda grass allergy. By contrast, these patients demonstrated an immuno-enhancing activity when tested for responsiveness to Bermuda grass. Studies to clarify and understand this disparity in suppression versus enhancement to Bermuda grass and ragweed are currently under investigation.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 83/37

STATUS: Ongoing

TITLE: Cardiopulmonary Effects of Stressful Exercise at 4,000 Feet on SCT Individuals

START DATE: Jul 84

ESTIMATED COMPLETION DATE: Jul 92

PRINCIPAL INVESTIGATOR: LTC Idelle M. Weisman

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Sickle cell trait, Stress, Hypoxia, Exercise

Study Objective: To establish baseline pulmonary function data (spirometry, helium dilution lung volumes, maximum voluntary ventilation L/min (MVV), arterial blood gas analyses (ABG), single breath diffusing capacity DLCO_{SB} (ml/min/mmHg) and steady state diffusing capacity DLCO_{SS} (ml/min/mmHg) (Fillee technique) as well as values for the partial pressure of oxygen at 50 saturation (mmHg) (P50) in HgbAS individuals and controls and to determine percent HgbS and percent HgbF in individuals heterozygous for sickle cell trait (HgbAS) at 4000 ft.

To carefully document cardiopulmonary response of individuals identified as having hemoglobin AS during both strenuous incremental and submaximal steady-state exercise at altitude with age, race, sex, smoking, matched non-HgbAS controls.

To correlate observed abnormalities (if any) in parameters of cardiopulmonary performance with levels of HgbS in individuals with sickle cell trait (i.e. are patients with 40 percent of HgbS more likely than controls to experience abnormalities during vigorous exercise. Also, to determine whether HgbF levels may be protective as they are in patients with sickle cell disease.

To determine whether conditioning (repeat studies after six weeks) is operative in modulating cardiopulmonary performance in both SCT individuals and controls.

Conclusive data is not anticipated from this protocol, but a preliminary statement or suggestion may be offered on the important question of occupational restriction of subjects with HgbAS. This is in keeping with the National Academy of Science - National Research Council Report of 1973.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Addendum (Mar 85): Added testing at 7,500 ft

Progress: 121 subjects were tested. Data collected at simulated 4,000 m (Phase III) is being reevaluated. If necessary 6 more subjects may still be added to this phase of the protocol.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 88/05

STATUS: Terminated

TITLE: IND Janssen Pharmaceutica #R51,211 Treatment of Systemic Mycoses with Itraconazole (Monitor: COL Ortiz)

START DATE: Oct 87

ESTIMATED COMPLETION DATE: Apr 91

PRINCIPAL INVESTIGATOR: LTC Idelle M. Weisman

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Itraconazole, Systemic mycoses

Study Objective: To assess the efficacy of Itraconazole therapy in fungal dissemination disease.

Technical Approach: The details are lengthy and specified in the Pharmaceutical Company protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Patient moved to New York City in Nov 90, but still receives Itraconazole through a New York physicians group. During his time in El Paso, his clinical status remained the same. His cocci titer remained positive (4+ at 1:4), negative coccidioidin skin test, normal CXR, unchanged GI exam. No adverse affects from Itraconazole.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 88/38

STATUS: Ongoing

TITLE: Comparison of Physiologic Responses to Prolonged Exercise Simulating Army Field Training in Sickle Cell Trait and Controls (Phase IVa) (Monitor: COL Michaels)

START DATE: Jul 89

ESTIMATED COMPLETION DATE: Jun 92

PRINCIPAL INVESTIGATOR: LTC Idelle M. Weisman

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: R. Jorge Zeballos, MD; COL John Little, ADA; CPT TW Martin, MC

KEY WORDS: Sickle cell trait, Endurance exercise

Study Objective:

1. To determine if submaximal (50-70% VO₂ max) prolonged treadmill exercise (1 hour 30 minutes) with a final maximum exercise (5 minutes), similar to Army field training conditions, would elicit differences in exercise performance between Sickle Cell Trait (SCT) and control volunteers.
2. To evaluate changes in Percent Sickling (%S) and blood viscosity with prolonged exercise in SCT volunteers and to analyze their relationship to venous oxygen saturation, hydration status and temperature.
3. To assess biochemical and enzymatic changes in blood and urine that would suggest muscle damage (rhabdomyolysis) during prolonged exercise.
4. To compare the effect of prolonged exercise on renal function in SCT and controls.
5. To determine whether subtle pulmonary microcirculatory abnormalities not present at rest would be detected during exercise in SCT compared to controls.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: 10 SCT/8 control patients have been entered into this protocol; desired number is 40. Data file has been created with 700 variables for each subject with cardiopulmonary, hematologic and biochemical data collected during 90 minutes of exercise. Statistical analysis of data is underway. Preliminary results will be used to determine if Phase IVa of the protocol will be modified or continue in the present form. An abstract is being prepared for submission to the 1991 American Thoracic Society (ATS) International Conference.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/68

STATUS: Ongoing

TITLE: In Vivo Sickling in Sickle Cell Trait (HbAs): Effect of Hypoxia, Exercise and Red Cell Sampling/Fixation Time

START DATE: Jul 89

ESTIMATED COMPLETION DATE: Jun 93

PRINCIPAL INVESTIGATOR: LTC Idelle M. Weisman

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: R. Jorge Zeballos, MD

KEY WORDS: Sickling, Sickle cell trait, Kinetics

Study Objective: Recent discoveries in Hemoglobin S (HbS) polymerization kinetics make it imperative to re-examine the sickling phenomenon in vivo in order:

1. To corroborate, by using a new, specially designed blood drawing technique, that in vivo sickling is present in the blood of individuals with Sickle Cell Trait.
2. To determine the effect of hypoxia on the magnitude of sickling.
3. To compare the combined effect of hypoxia and exercise on sickling measured in effluent blood from an exercising limb and in arterial blood that has recirculated through the lungs during leg exercise.
4. To determine the effect of red cell sampling/fixation time on the measurement of percent sickling.

Technical Approach: The study will be carried out in the Human Performance/SCT Laboratory at William Beaumont Army Medical Center in El Paso, Texas at an altitude of 1270m and mean barometric pressure of 656mm Hg.

Ten individuals with SCT will be used for this study. All will be between 18 and 28 years of age and will be non-smokers. Volunteers will be obtained from the basic training reception station at Logan Heights, Ft Bliss, Texas similar to previous studies (WBAMC 83/37, WBAMC 88/38). All incoming recruits are screened for SCT with a Sickledex test; positive results will be confirmed by cellulose acetate (pH=8.4) hemoglobin electrophoresis with % HbS determined by quantitative scanning densitometry. Individuals identified as possessing SCT (HbAS) will be asked to participate in the study after an explanation of the protocol, including its purpose, risks and benefits by one of the researchers. Based on past experience, between 30-50% of basic trainees with SCT volunteer to participate. In addition, SCT counseling will be provided by LTC Weisman. This remains important because >70-80% of basic trainees with SCT do not know that they have HbAS or what it means to be positive for HbAS. If the individual with SCT agrees to volunteer in the study, he or (they) will be transported to the SCT lab. Upon arrival, the subjects will read the volunteer agreement and ask any remaining questions. We will explain that they may withdraw from the study at anytime without penalty. If the volunteer withdraws, he will be transported back to his original unit. The NCO will not be informed of the circumstances surrounding the trainee's return. Usually within hours, the former volunteer and the rest of his unit is transferred to a training battalion and a new NCO.

After obtaining informed consent, documented in writing, a physical examination will be performed on each volunteer, and a medical history will be obtained. Baseline EKG, CBC, Urinalysis and SMA-20 will be obtained/checked. If the subject has no contraindication to exercise, he will be accepted into the study. Controls are not necessary for this study.

A 20 gauge venous catheter (3.2 cm length, Quick Cath, Travenol Labs) will be inserted into one of the median antecubital veins of the exercising arm of each volunteer. If an Allen's test reveals a palmar blush within five seconds, a second 20 gauge catheter (Becton, Dickinson) will be placed in the radial artery of the non-exercising arm. Using this technique in over 150 arterial catheter insertions, we have had no ischemic complications; all volunteers have successfully completed basic training. Approximately 30-40% of subjects have

experienced minor wrist discomfort which typically resolved within 24 hours without sequelae. No other complications have occurred. Previously approved WBAMC Protocol 88/38 fully discusses the risks of catheterization. The patency of the catheters will be maintained using a heparin flush solution (10 USP unit/ml) intermittently. Blood samples will be drawn anaerobically for blood gas analysis and percent sickling measurements at rest and during exercise.

This is a simplified version of previously approved WBAMC protocols 83/37 ("Cardiopulmonary Effects of Stressful Exercise at Altitude (4000ft) of Individuals with Sickle Cell Trait (SCT) with modification to include altitudes of 2300m and 4000m") and WBAMC 87/25 ("Axillary Venous Sickling in Individuals with Sickle Cell Trait During Upper Extremity Exercise in a Hypoxic Environment").

The subjects will be studied at rest breathing room air ($\text{FIO}_2 = 21\%$, $\text{PIO}_2 = 127\text{mmHg}$) and then breathing a hypoxic gas mixture ($\text{FIO}_2 = 14\%$, $\text{PIO}_2 = 85\text{mmHg}$) equivalent to 4000m for 15 minutes at rest (before the exercise) and during the exercise tests. The hypoxic gas will be administered via a respiratory gas mask during rest and hand grip exercise and a mouth piece during leg exercise. The inspiratory port of both devices will be connected to a 120L reservoir bag continuously fed from the gas cylinder with the hypoxic gas.

Two types of exercise formats will be used:

a) Hand Grip Exercise: After 15 minutes of breathing the hypoxic gas mixture, the subjects will first perform a maximum rhythmic hand grip exercise at a rate of 60 grips per minute, pulling a weight of 16 pounds from an apparatus, consisting of a hand grip cable, pulley and adjustable weights. The exercise will be performed only with the arm in which the venous catheter has been placed. The duration will be approximately 3 minutes.

b) Leg Exercise: After 15 minutes of breathing the hypoxic gas mixture at rest, the subjects will be exercised on an electronically braked cycle ergometer. The exercise test will consist of two stages of steady state exercise consisting of 5 minute duration each. The first stage will be at 50%, and the second at 75% of the maximum power predicted for each individual. During the cycle exercise test, minute ventilation (VE), oxygen uptake (VO_2), carbon dioxide production (VCO_2), and respiratory exchange ratio (R) will be measured in a breath-by-breath fashion using a computerized system (Medical Graphics Corporation) that integrates flow (pneumotachometer) with the respiratory gases measured continuously in the mouthpiece with a mass spectrometer (Perkin-Elmer). Heart rate (HR) and electrocardiographic changes will be monitored continuously during the exercise tests with an Electrocardiographic System. The arterial blood gas results will be entered in the computer and the physiologic dead space-tidal volume ratio (VD/VT) and the alveolar-arterial oxygen pressure difference [P(A-a)O_2] will be calculated.

A short IV extension tube attached to a drawing apparatus will be connected to either the venous or the arterial catheter. The apparatus consists of the following elements: (a) a 3-way stopcock connected in series with (b) a one-way back pressure valve placed between the venous catheter and the port where (c) the syringe with the 1% glutaraldehyde phosphate buffer solution will be connected (a 6cc plastic syringe will hold the glutaraldehyde solution). A (d) plastic safety sleeve will be placed around the plunger and then marked with (e) a red ring. The 1% glutaraldehyde solution is a biological fixative used for fixing blood cells. If this solution is injected into the subject, it could induce serious medical complications. To our knowledge, there is no literature available about the effect of accidental injection of glutaraldehyde into a human being.

The drawing apparatus has been tested for safety by the Clinical Pharmacist of the Hematology/Oncology Service, WBAMC (see attached report). It would appear that this apparatus/technique approaches almost complete freedom from the possibility of accidental injection of the fixative into the subject; This possibility is even less likely if used by a researcher who is familiar with the system. Another important safety feature is that during the blood sampling, all the maneuvers that are required will be that of pulling the plunger, and never that of pushing or injecting.

Arterial and venous blood samples will be taken at rest breathing room air, at rest breathing the hypoxic gas mixture (14% FIO_2), and at the end of the hand grip and leg exercises, while breathing the hypoxic gas mixture. The blood samples will be drawn and then fixed immediately in the fixative solution (<2sec); Immediately thereafter, another blood sample will be collected into a heparinized syringe. This syringe will then be removed from the drawing apparatus, and the blood fixed in glutaraldehyde solution at 30, 60, 180, and 300 second intervals, while being maintained in an anaerobic environment at 37°C. At the end of the Exercise test, the catheters will be removed.

Blood gas analysis will be performed on all samples collected including those used for the measurement of Percent sickling. Oxygen tension, carbon dioxide tension and pH will be measured in an automated blood gas analyzer (IL) and oxygen saturation in a spectrophotometric oximeter (IL CO-Oximeter).

After fixation of the blood samples, slides will be prepared from one to two drops of the glutaraldehyde-red cell suspension and examined under a phase contrast microscope. A thousand cells from random areas of the preparation will be photographed for determination of percent sickling (number of sickled cells per 100 counted). Sickling will be determined independently and in a blind fashion by two observers. A cell will be considered sickled if it is elongated with at least one or two projections or if it is irregularly shaped with an angle and one or more points (21). Ovalocytes, tear drops, echinocytes, and other poikilocytes will be excluded. These criteria for sickling morphology have been adopted and vigorously applied in our lab (22).

An ACLS-qualified physician will monitor the patient's clinical status during the test. Testing will be interrupted if the patient experiences significant discomfort (abdominal pain, muscle cramps) or if a dysrhythmia is noted. A crash cart, supplemental oxygen and defibrillator will be available at all times. In over 150 prior cycle exercise tests with hypoxia we have had no significant complications. We anticipate the catheters will be in place for no longer than two or three hours. After the tests are completed, the catheters will be removed immediately and direct pressure will be applied to the site. A stat vascular surgery consult will be obtained in the unlikely event that a subject develops signs of ischemia.

Progress: Two more volunteers were studied. Preliminary statistical analysis has been performed. To determine more precisely the percent of Sick cells present in peripheral venous blood of SCT individuals under adverse environmental conditions, 5 more subjects will be studied using the technique for immediate blood fixation. Preliminary results were presented in the Laboratory of Chemical Biology at the National Institute of Health in Bethesda, MD (Jul 91).

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 88/62

STATUS: Completed

TITLE: Armcrank and Cycle Exercise in the Evaluation of Dyspnea (Monitor: COL Ortiz)

START DATE: Jul 88

ESTIMATED COMPLETION DATE: Jul 91

PRINCIPAL INVESTIGATOR: Jorge Zeballos MD

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Idelle M. Weisman, MC

KEY WORDS: Armcrank, Cycle exercise

Study Objective: Compare the cardiopulmonary response to armcrank and cycle exercise in subjects with dyspnea on exertion.

Technical Approach: We will use 20 male or female patients, 18-65 years old, referred to the pulmonary department for evaluation of dyspnea on exertion. These patients routinely undergo cycle exercise testing with an arterial line in place. Subjects will be excluded if they have orthopaedic, neurologic, or vascular abnormalities which limit arm or leg exercise.

Subjects will perform both upper and lower extremity exercise on an electronically braked cycle ergometer. For the upper extremity test, the cycle will be placed on a table so that the crank shaft will be level with the seated patient's shoulders. The order of the tests will vary so that a similar number of subjects begin with either arm or leg exercise. Beginning with no added resistance or 0 watts, the work rate will increase 10-20 W/min until the subject is unable to maintain a 60 rpm crank rate. The test will also be discontinued if the subject has ventricular tachycardia, more than a 20mm drop in systolic blood pressure, or >3 mm ST depression.

While exercising, the subjects will breathe through a two-way valve. We will measure respiratory gases at the mouthpiece using a mass spectrometer (Perkin Elmer). Ventilation will be measured with a pneumotachometer (Hans Rudolph). An on-line computer (MGC 2001) will perform breath-by-breath calculation of O_2 uptake ($\dot{V}O_2$), CO_2 production ($\dot{V}CO_2$), minute ventilation (VE), and other measurements. We will monitor heart rhythm on an oscilloscope and measure heart rate from a rhythm strip obtained during the last five seconds of each minute.

One hour before the first exercise test, a 20 gauge catheter will be inserted in the patient's radial artery. A 25cm tube with a three-way stopcock will be attached to the catheter to permit anaerobic sampling while the subject exercises. Patency of the catheter and connecting tube will be maintained with a heparin solution (10 USP unit/ml).

We will draw blood samples with the subject at rest and every 2-4 minutes during exercise. We will measure PO_2 , PCO_2 , and pH with an automated blood gas analyzer (IL System 1303). Hemoglobin saturation and concentration will be measured with a spectrophotometric oximeter (IL 282 CO-Oximeter). The dead space-tidal volume ration and the alveolar-arterial oxygen difference will be calculated using standard equations.

Progress: No additional patients have been entered into this protocol since last abstract (19 patients total have been entered). There have been no withdrawals or adverse reactions to report. Data is being collected for comparison with another study.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/48

STATUS: Ongoing

TITLE: Practical Value of Hyper-Reactive Airway Testing in the Assessment of Asthma in Army Recruits
(Monitor: COL Michaels)

START DATE: Aug 89

ESTIMATED COMPLETION DATE: Jun 93

PRINCIPAL INVESTIGATOR: R. Jorge Zeballos MD

DEPARTMENT: DCI

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Idelle M. Weisman, MC

KEY WORDS: Asthma, AIT, Army recruits, Reactive airway disease, Bronchial challenges

Study Objective:

1. To determine whether a screening test for hyperreactive airways "asthma" should be established for individuals who, although having met entry requirements as specified in AR 40-501-2-24d have allergic histories and/or a history of asthma in childhood (HAC), which would appear to increase their likelihood of exercise induced asthma and other asthma related problems during basic training.
2. To determine which of the currently available methodologies, for the diagnostic evaluation of hyperreactive airways, would be most accurate (high sensitivity, high specificity), practical, and cost effective for the screening of potential Army recruits.
3. To modify standard methods for the diagnosis of airway hyperresponsiveness so as to make them more suitable to the Military Entrance Processing Service (MEPS).
4. To propose modification for AR40-501-2-24d based on the results of this study and thereby reduce the number of Existing Prior to Service (EPTS) discharges secondary to asthma.

Technical Approach: All incoming basic trainees at Ft. Bliss will be asked to respond to a questionnaire which will identify the inclusion criteria: (1) history of allergic rhinitis (hay fever), and/or (2) history of allergic dermatologic disorder (i.e., eczema), and/or (3) history of asthma in childhood and (4) normal or border line pulmonary function tests. Service members responding affirmatively to any of the inclusion criteria will be asked to participate in the study.

A physical examination will be performed on each volunteer, and a medical history will be obtained. Baseline EKG, CBC, Total Eosinophil count, and SMA-20 will be obtained/checked.

The study will be conducted on 2 consecutive days in the Human Performance/ Pulmonary Function Labs at WBAMC. On the first day, the exercise induced broncho- constriction test will be performed in the morning, followed by the nebulized distilled water test in the afternoon. On the second day, the hyperventilation with cold air test will be performed in the morning, followed by the nebulized metacholine test in the afternoon. The pulmonary functions at baseline for each test should not differ by more than 5%. The volunteers will be followed during their stay at Ft. Bliss (at least 7-8 weeks) and even longer for those SM's assigned here for AIT. All admissions to a hospital for 48 hours or more, failures to pass the Army Physical Fitness Test, or discharge from the service (especially with a principal diagnosis of asthma) will be carefully documented. A relationship between positivity to hyperreactive airway tests and medical problems related to asthma will be analyzed.

An ACLS-qualified physician will monitor the patient's clinical status during all the testing. Testing will be interrupted if the patient experiences significant chest tightness, wheezing, shortness of breath, chest pain, or if a dysrhythmia is noted. A crash cart, supplemental oxygen and defibrillator will be available at all times.

Progress: Ten patients have been enrolled to date; desired number is 25. Since basic training at Ft. Bliss was terminated, volunteer recruitment has been very difficult. A new system is being established to recruit volunteers from AIT.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/30

STATUS: Completed

TITLE: A Psychosocial View of Health Care: Where Health Care has been and Its Destination in the Army

START DATE: Apr 91

ESTIMATED COMPLETION DATE: Jun 91

PRINCIPAL INVESTIGATOR: MAJ Peter K. Moskowitz

DEPARTMENT: CSD

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Health care

Study Objective: To search the history of health care as an indicator for future trends.

Technical Approach: Research literature and review past, present and future prospects of health care.

Progress: Project completed and paper submitted for local DCI competition. Accepted for publication in *Futurics*.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/75

STATUS: Ongoing

TITLE: Comparison of Cranial and Iliac Autologous Bone Grafts and their Effect on the Success Rates of Subsequent Osseointegrated Intra/Extraoral Implant Application in the Miniature Swine

START DATE: Mar 89

ESTIMATED COMPLETION DATE: 2 Feb 90

PRINCIPAL INVESTIGATOR: LTC Nathan C. Dickerson

DEPARTMENT: Dentac

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Michael G. Donovan, DC; MAJ Jan Faulk, DC

KEY WORDS: Cranial bone graft, Iliac bone graft

Study Objective: PHASE I: Design surgical techniques for harvesting bilateral iliac corticocancellous bone grafts, and cranial bone and cranial-facial flap techniques.

(a) Study will provide knowledge for surgical techniques that will minimize morbidity (pain, muscular dysfunction, nerve damage) in swine for future studies.

(b) Phase I study will be performed on one (1) domestic swine prior to bone graft studies (Phase II and Phase III) on more expensive miniature swine.

PHASE II: Compare traditional reconstruction techniques, autologous iliac bone grafts, with autologous cranial bone grafts in maxillofacial reconstruction. Will verify if cranial bone is superior to iliac bone in maxillofacial reconstruction. Facial onlay bone grafts and continuity defect repairs are to be compared.

(a) Will compare rate of revascularization and magnitude of resorption at different time intervals for cranial and iliac bone grafts.

(b) Will evaluate need for donor bone graft to duplicate recipient site.

PHASE III: Will determine degree of osseointegration of pure titanium bone implants in cranial and iliac bone grafts in:

(a) Intraoral continuity defects

(b) Extraoral continuity defects

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Phase I of the project was completed November 1989 with evidence that the swine is a good surgical model for comparison of cranial and iliac bone grafts to the facial bones.

Phase II: All grafted bone was found to be viable. The calvarial onlay bone grafts had a greater percentage of retention of 84.5% at six to twelve months compared to only 35.6% for the iliac onlay grafts. The calvarial bone grafts were found to have a greater density by more than twofold compared to iliac bone grafts. Conclusion: Calvarial bone is superior to iliac bone for onlay grafts due to the greater retention of the grafted bone volume. Retention of these onlay bone grafts was not because of revascularization of the grafts, but because of the greater density of calvarial bone compared to iliac bone.

Phase III, placement of Branemark osseointegrated implants into previous cranial bone grafts is progressing as planned. Radiographic studies have been completed and the final view of the Titanium and Onlay Bone Interface with SEM is pending.

Presented at the Oral and Maxillofacial Surgery Association national meeting in September 1991.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/20

STATUS: Ongoing

TITLE: Comparison of Osseointegration of Titanium Implants in Cranial and Iliac Autologous Bone Grafts Stabilized with Immediate Titanium Implant Fixtures in Miniature Swine

START DATE: May 91

ESTIMATED COMPLETION DATE: Feb 92

PRINCIPAL INVESTIGATOR: LTC Nathan C. Dickerson

DEPARTMENT: Dentac

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Michael G. Donovan

KEY WORDS: Titanium implants, Bone grafts

Study Objectives:

1. Examine time interval of osseointegration of titanium implants when placed in immediate bone grafts.
2. Compare the rate of osseointegration, i.e., success rate, of titanium implants in immediate autologous calvarial and iliac bone grafts.
3. Compare the rate of osseointegration, i.e., success rate, between immediate placement of titanium implants in grafted bone to titanium implants in mature bone grafts.
4. Determine the recommended time interval of osseointegration required prior to placement of functional load on implants.

Technical Approach: Six miniature swine will be used for this study. Each animal will serve as its own control by having an implant placed in a non-grafted facial bone site.

Under general anesthesia, each swine will have autologous bone from the outer table of the frontal and parietal bones harvested and a corticancellous bone graft from the iliac crest harvested. Placement of the bone grafts will be to the nasal bones of the swine. The bone grafts will be rigidly fixed utilizing one or more Branemark titanium implant fixtures of 7mm or 10mm lengths. Four calvarial bone grafts and four iliac bone grafts will be utilized on each animal. The calvarial bone grafts will be on the right side and the iliac bone grafts will be on the left side of the nasal bones.

One swine will be euthanatized at one month, two months, four months, six months, eight months, and twelve months to obtain specimens for histological studies. Twenty-one days prior to scheduled euthanation and biopsy, the animals will be marked with an I.M. injection of a tetracycline derivative to assess new bone growth in the bone grafts adjacent to the implant fixtures. Barium sulfate mixed with heparinized formalin will be infused after euthanasia to mark neovascularization in the bone grafts.

Each bone graft site will be physically measured for evidence of bone resorption or growth, and these measurements will be compared with the dimensions of the bone grafts measured at time of initial placement. The titanium implants are of fixed length and will serve as markers for loss or maintenance of the bone graft heights along with the above physical measurements.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Three animals have undergone surgery for autologous bone graft harvesting and placement and Branemark titanium implants placed. No adverse reaction/morbidity noted. The remaining subjects are scheduled for surgery in November/December 1991 with necropsy beginning in December 1991. Louisiana State University Maxillofacial Surgery Service and Residency has acquired the machine to cut the specimens and implants from scanning of interface with electron microscopy and samples of specimens will be sent to them.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/37

STATUS: Ongoing

TITLE: Bone-Anchored Craniofacial Prostheses Investigation

START DATE: Oct 89

ESTIMATED COMPLETION DATE: Dec 91

PRINCIPAL INVESTIGATOR: COL Michael G. Donovan

DEPARTMENT: Dentac

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL John Gary, MC

KEY WORDS: Craniofacial prostheses, Bone-anchored prostheses

Study Objective:

1. To evaluate the long term retention success rate for titanium implants anchoring craniofacial prostheses.
2. To evaluate the long term stability of the prostheses.

Technical Approach: Patients will be admitted to Ward 6W, and have the routine pre-surgery laboratory studies, to include blood work, x-rays and urinalysis, and any further tests required that would be dictated by their medical history. Appropriate referrals will be given to various medical specialties if indicated. The surgery to implant the prosthesis will be conducted in the operating room. Anesthetic will be given to minimize the pain that is associated with any surgical procedure. The doctor will cut the skin covering the area to be treated and then drill holes in the bones of the face, head, or both. Next, tiny titanium fixtures will be inserted into the holes, the skin will be replaced so that it covers the fixtures, and the skin stitched. The titanium fixtures will be left in place for 3-4 months to allow them to become integrated with the bone. During this time the patient will visit the doctor 2-3 more times so their condition can be monitored.

After 3-4 months, the patient will once again be admitted to the hospital, where they will undergo additional surgery. After the anesthetic is administered, the doctor will again cut the skin covering the area being treated. Some of the tissue under the skin will be removed and the skin will be stitched back together. The doctor will then puncture the skin directly over each implanted titanium fixture and will attach a small skin-penetrating abutment to each fixture. For 3-4 weeks, the treated area will be allowed to heal. During that time the patient will visit their physician 1-3 times so that their condition can be monitored.

After 3-4 weeks, a prosthesis will be made and will be attached to the anchors. After the prosthesis is in place, the patient will continue to visit their physician 3 times during the first year, then twice a year, so that their condition can be monitored, as well as their level of satisfaction.

Progress: Four patients have had a total of thirteen implants placed. One of the thirteen implants failed to integrate and was removed without sequelae and did not affect the outcome of the treatment. Three patients completed the active phase of treatment and have had their prosthesis placed. One patient received a prosthetic ear, one patient received a prosthetic nose and the third patient received an orbital prosthesis. All are doing well in their followup phase. The fourth patient has had three implants placed in his left mastoid bone and now awaits the second phase of treatment to uncover the implants for placement of a prosthetic ear. A fifth patient is awaiting evaluation prior to placement of the implants for replacement of a missing ear.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/19

STATUS: Completed

TITLE: A Study of Antimicrobial Properties of Impression Tray Adhesives

START DATE: Mar 91

ESTIMATED COMPLETION DATE: Mar 91

PRINCIPAL INVESTIGATOR: MAJ David A. Herman

DEPARTMENT: Dentac

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Adhesives, Antimicrobial

Study Objective: The main objective of this project is to see if any of the impression tray adhesives possess antimicrobial properties. If the antimicrobial property is evident, this secondary effect of disinfection will make the possibility of material and patient cross-contamination less likely. The object is not to determine the most powerful antimicrobial adhesive, but to see if the chemicals present in the adhesives will mimic their organic compound counterparts present in disinfectants.

Technical Approach: Freeze-dried cultures of *Pseudomonas aeruginosa*, *Salmonella choleraesuis*, and *Staphylococcus aureus* will be rehydrated and transferred to a test tube of recommended broth. After a few days, cultures will be grown out and transfer dilution will be made.

The two testing methods are dilution plating and filter paper disk inhibition. The dilution plating method consists of application of a suspension of bacteria to the adhesive layer painted on the sterile plastic petri plate. The solution is collected after 20 minutes and then plated on tryptic soy agar blood plates and incubated for 48 hours. Then the colonies will be counted. The filter paper disk inhibition method consists of applying the disk saturated with the impression tray adhesive to the plated bacteria cultures on tryptic soy agar blood. The plates will be incubated and observed at 24, 48, and 72 hours for measurement of any inhibitory zones.

The three impression tray adhesives include Coe adhesive (Coe Laboratories, Inc.), Express tray adhesive (3M Company), and Hold adhesive (Teledyne Getz/Densco). These adhesives were chosen since they represent three common and chemically distinct impression material systems widely used in dentistry. The bioburden is added to the bacterial culture dilution as a 50:50 vol/vol mixture.

Each testing procedure will have the same three organisms and same three impression tray adhesives plated with and without the human blood bioburden in these various combinations five times each.

Amendment: The testing method was amended to putting 0.5ml of an estimated bacterial suspension in a 5ml adhesive/mineral oil mixture and letting it react for 30 minutes. After that, successive dilutions are made until the estimated dilution is plated at 0.1ml on TSA blood plates by the dilution plating method. The plates are incubated for 24 hours and then colonies are counted. Five dilution samples will be made for each adhesive/bacterial test sample and three platings will be made from each of these five dilutions.

Progress: Three common impression tray adhesives were tested for their antimicrobial actions on three bacteria strains used for disinfectant studies. The colony forming units (CFU) counts from plating the adhesive-exposed bacteria showed a significant reduction in number compared to the CFU of the controls.

Conclusion: Statistical analyses confirmed the significant reduction (p less than 0.05) for all but one test case. Proper infection control procedures should always be followed, but the added benefits of disinfection by impression tray adhesives can help prevent cross-contamination. Submitted for publication.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/41E

STATUS: Completed

TITLE: Emergency Use of Azithromycin (Patient J.C.)

START DATE: Jun 91

ESTIMATED COMPLETION DATE: Jul 91

PRINCIPAL INVESTIGATOR: MAJ Naomi E. Aronson

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Azithromycin, Lyme Disease

Study Objective: Emergency use sought for treatment of patient whose recent partial synovectomy (FAMC) showed the persistence of spirochetes. Patient flaring despite chronic doxycycline and not responding well to intravenous ceftriaxone.

Technical Approach: Azithromycin administered IAW Pfizer protocol #066-127 (IND #24,999).

Progress: Subject's participation in this protocol was terminated after discussion with Dr. Johnson, Pfizer Research Medical Monitor. IND agent given for prescribed 14 days. Ten days off therapy, patient demonstrated progression shown by WSR elevation, fever, new left MCP arthritis and swelling/effusion/tenderness of right knee. Patient suffered no adverse reactions while taking Azithromycin and her WSR normalized on therapy.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/41

STATUS: Terminated

TITLE: Use of Azithromycin in a patient with Lyme Disease who has failed conventional antibiotic therapy (COL Cannady)

START DATE: Jul 91

ESTIMATED COMPLETION DATE: Nov 91

PRINCIPAL INVESTIGATOR: MAJ Naomi E. Aronson

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ David Slagle

KEY WORDS: Azithromycin, Lyme Disease

Study Objective: To assess the safety and efficacy of Azithromycin therapy in refractory stage III Lyme Disease under

Technical Approach: Treatment IAW Pfizer protocol #066-127 (IND #24,999). The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Protocol was terminated after discussion of emergency use results with Dr. Johnson, Pfizer Research Medical Monitor.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/38

STATUS: Terminated

TITLE: Cost-Benefit Analysis of Routine, Right-Sided Cardiac Catheterization in the Evaluation of Coronary Artery Disease by Left-Sides Catheterization

START DATE: Aug 90

ESTIMATED COMPLETION DATE: Aug 91

PRINCIPAL INVESTIGATOR: CPT Terry D. Bauch

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ William A. Collazo, MC; MAJ Thomas Stoughton, MC

KEY WORDS: Cardiac catheterization, Coronary artery disease

Study Objective: This study examines the question of whether routine right-sided cardiac catheterization is justified in the evaluation of coronary artery disease by left-sided catheterization. Military beneficiaries already scheduled for left heart catheterization will be studied in a prospective fashion.

Technical Approach: A right-heart catheterization will be performed on 200 consenting adults of both sexes, ages 20 to 90, already scheduled for left-heart catheterization in the evaluation of known or suspected coronary artery disease. The study will not be blinded. Exclusion criteria include known or suspected pulmonary or right-heart pathology as identified by historical, physical, and non-invasive laboratory findings. The patients thus excluded will include those with congestive heart failure, myocardial disease, pericardial disease, and significant valvular heart disease. A normal right heart catheterization performed within the previous 12 months will also be an exclusion criteria. Routine right-heart hemodynamic data will be recorded to include right atrial and ventricular pressures, pulmonary artery pressure, pulmonary capillary wedge pressure, cardiac index, and superior vena caval and pulmonary arterial oxygen saturations. Standard left heart catheterization data will also be obtained. Given the prior practice of routine right heart catheterization in our laboratory, the patient will not be subject to additional risk by study participation. Subjects are terminated if right-heart catheterization is normal. The remainder are followed through the secondary evaluation of the abnormalities elicited. The outcome of secondary evaluation will be noted, and a cost-estimate made for the additional work. Cost-benefit will be judged by comparing the health care costs of early identification of unsuspected abnormalities versus the estimates of cost should these abnormalities have not been found.

Progress: Protocol was terminated due to PSC of the PI and an AI. During the course of the study, no adverse effects were noted.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/22

STATUS: Ongoing

TITLE: Fourth International Study of Infarct Survival (ISIS-4)

START DATE: Jun 91

ESTIMATED COMPLETION DATE: Aug 93

PRINCIPAL INVESTIGATOR: CPT Barrett L. Chapin

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Carolyn Bernheim, MAJ Roger Belbel

KEY WORDS: Infarct Survival, Captopril, Magnesium, Nitrate

Study Objective: To obtain reliable assessment of the separate and combined effects on vascular mortality of adding three widely practicable treatments to the current standard treatments for a wide range of types of patient (high risk and low risk) with definite or suspected myocardial infarction.

Technical Approach: This will be an international, multi-center, partially double-blinded, partially placebo-controlled, randomized, prospective study. The three study treatments will be randomized in a "2 x 2 x 2 factorial" design. Each patient will be randomized between controlled-release mononitrate vs. placebo, captopril vs. placebo, and magnesium vs. open control. If, as hoped, a total of 40,000 patients is randomized, there will be about 5000 patients in each of the eight possible combinations of trial treatment. The eight possible combinations are: 1) nitrate alone, 2) captopril alone, 3) magnesium alone, 4) nitrate and captopril, 5) nitrate and magnesium, 6) captopril and magnesium, 7) nitrate, captopril, and magnesium, and 8) no trial treatment. Group sizes of 5000 may not be large enough to yield statistically reliable results. But, the factorial design makes the assumption that the effect of the other two trial treatments is equally distributed between the treatment of interest and its control due to the randomization. Therefore, if 40,000 patients are entered, each treatment will have 20,000 patients vs. 20,000 control subjects for data analysis.

Progress: The study commenced in Aug. Two patients have entered the study. For the entire ISIS study, it is hoped that 40,000 patients will be randomized to the three treatment arms. The end points are mortality at one month or in hospital. There have been no problems, adverse effects, or withdrawals.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/31

STATUS: Completed

TITLE: Health Status Awareness Survey

START DATE: May 90

ESTIMATED COMPLETION DATE: Oct 91

PRINCIPAL INVESTIGATOR: MAJ Christopher P. Cheney

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Harry E. Davis, COL, MC

KEY WORDS: Health Status Assessment Questionnaire

Study Objectives:

1. Assess patients' awareness of their medical problems.
2. Assess patients' awareness of how their current problems will impact on their future health status.
3. Identify patients' life styles and habits that impact on their health.
4. Survey the patients' insight and/or attitudes regarding care provided by the clinic.
5. Elicit suggestion as to how to improve the efficiency and operation of the Internal Medicine Clinic (IMC).

Technical Approach: The study will survey outpatients of the IMC over two calendar months. The questionnaire will be given to all patients as they sign in to our clinic and who meet our inclusion criteria. They will be encouraged to fill out the questionnaire while they are waiting for their appointment, or return it to the clinic as soon as possible via a self addressed envelope. Their responses to all questions will be encouraged. Our goal is to obtain over 500 completed questionnaires. The questionnaire evaluates a series of general medical problems seen frequently in the IMC to include tobacco abuse, alcohol abuse, hypertension, hypercholesterolemia, coronary artery disease, cancer screening and obesity. The questions address whether the patient is aware of their diagnoses, are they aware of how various life styles affect the natural history of the disease and do they know means available to lessen or eliminate the disease.

Progress: Five hundred questionnaires were handed out over a six week period in the Internal Medicine Clinic. Of the 153 questionnaires (76 male and 77 female), 55% stated they received yearly flu shots. In this population, 96 of the 153 patients were >65 yo and of those patients, 67% claimed to have received their vaccination. When analyzed regarding smoking history, 9% currently smoked, 61% smoked in the past, and 20% had a diagnosis of COPD listed in their medical record. In these high risk patients, there was a 36% vaccination rate (VR) in the current smokers, a 68% VR in prior smokers and a 70% VR in those with COPD. In patients who elected not to receive the flu vaccine, the reasons for not obtaining one were varied but could be broken down into two broad groups, adverse reaction (40%) and inadequate patient education (60%). The biggest reasons stated included, it causes side effects (19%), it gives you the flu (17%), or it is not necessary (17%). In summary, in an internal medical clinic where the cost of obtaining a flu shot is not a barrier, the objectives of the 1980 Public Health Service have been met in certain groups at high risk. More emphasis on patient education is needed on those who continue to smoke and those who are misinformed regarding the reasons for vaccinations. Two talks are to be presented at the Army's American College of Physicians program in San Francisco in October 1991.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 84/35

STATUS: Terminated

TITLE: Adjuvant Chemotherapy with 5-FU, Adriamycin and Mitomycin-C (FAM) vs Surgery Alone for Patients with Locally Advanced Gastric Adenocarcinoma (SWOG 7804) (Monitor: LTC W. Lane)

START DATE: Mar 78

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Adenocarcinoma, Stomach, Adjuvant chemotherapy vs surgery

Study Objective: To determine the efficacy of adjuvant chemotherapy with 5-Fluorouracil, Adriamycin and Mitomycin-C (FAM) on the disease-free interval and survival of patients with TNM stage-groups IB, IC, II and III gastric adenocarcinoma compared to potentially curative surgery alone.

Technical Approach: The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: There have been no subjects entered into this study at WBAMC. The study was closed soon after the new gastric adjuvant study (SWOG 9008) opened.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 87/41

STATUS: Terminated

TITLE: SWOG 8600 Randomized Investigation of High Dose vs Standard Dose Cytosine Arabinoside with Daunorubicin in Patients with Acute Nonlymphocyte Leukemia (Monitor: LTC W. Lane)

START DATE: Nov 86

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Nonlymphocyte leukemia

Study Objective: To compare, among patients with acute nonlymphocytic leukemia, the rate of complete remission produced by induction regimens of either standard dose cytosine arabinoside and daunorubicin or high dose cytosine arabinoside and daunorubicin. To compare the duration of complete remission and of disease-free survival among patients who each receive one of three combinations of induction and consolidation regimens: Standard dose cytosine arabinoside and daunorubicin for both induction and consolidation. Standard dose cytosine arabinoside and daunorubicin for induction followed by high dose cytosine arabinoside and daunorubicin for consolidation. High dose cytosine arabinoside and daunorubicin for both induction and consolidation.

To determine the comparative toxicities of these three programs of induction and consolidation.

To determine the feasibility of implementing a predetermined approach to supportive care within a multi-institutional cooperative group setting for patients receiving intensive chemotherapy for acute nonlymphocytic leukemia.

Technical Approach: The details are lengthy and specified in the SWOG protocol. Duplicates are kept in the Department of Clinical Investigation and are available upon request.

Progress: There have been no patients entered into this study at WBAMC. Study terminated at WBAMC due to lack of support personnel.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 87/47

STATUS: Terminated

TITLE: SWOG 8598 Prospective Trial for Localized Cancer of the Esophagus (Monitor: LTC W. Lane)

START DATE: Oct 86

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Cancer, esophagus

Study Objective: Determine the role of chemotherapy for a potentially curable subset of patients with squamous cell cancer of the esophagus. Specifically to determine if the combination of chemotherapy and radiation will add to the overall survival and cure of patients treated with the combination when compared to patients treated by radiation alone. Determine if the patterns of recurrence for patients treated with the combination of chemotherapy and radiation differs from those patients treated with radiation alone.

Technical Approach: The details are lengthy and specified in the SWOG protocol. Duplicates are kept in the Department of Clinical Investigation and are available upon request.

Progress: There have been no patients entered into this study at WBAMC. Study closed in May 91.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 87/75

STATUS: Terminated

TITLE: SWOG 8694 A Comparison of Pentostatin (NSC-218321) and Alpha-Interferon (NSC-377523) in Splenectomized Patients with Active Hairy Cell Leukemia (Monitor: LTC W. Lane)

START DATE: Feb 87

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Hairy Cell Leukemia

Study Objective: To compare the frequency of response between pentostatin and a-IFN treatment in patients with hairy cell leukemia who following splenectomy manifest active or progressive disease. To compare time to response between these two treatments. To compare the response duration of these two treatments.

To determine whether pentostatin salvages nonresponders to a-IFN treatment and whether a-IFN salvages nonresponders to pentostatin treatment. To compare the toxicity of the two treatments.

Technical Approach: The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: There have been no patients entered into this study at WBAMC. Study terminated at WBAMC due to lack of support personnel.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 87/77

STATUS: Terminated

TITLE: SWOG 8792 Phase III Study of Alfa-nl (Wellferon) as Adjuvant Treatment for Resectable Renal Cell Carcinoma (Monitor: LTC W. Lane)

START DATE: Jun 87

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Renal Cell Carcinoma

Study Objective: To assess in a controlled fashion the effectiveness of Interon alfa-nl (Wellferon) as a surgical adjuvant in patients with renal cell carcinoma. Study endpoints will consist of patient survival and time to recurrence.

Technical Approach: The details are lengthy and specified in the SWOG protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: There have been no patients entered into this study at WBAMC. Study terminated at WBAMC due to lack of support personnel.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/29

STATUS: Terminated

TITLE: SWOG 8624: A Phase III Randomized Trial of Combination Therapy for Multiple Myeloma. Comparison of (1) VMCP/VBAP to VAD or VMCP/VBAPP for Induction; (2) Alpha-2b Interferon or No Therapy for Maintenance; and (3) Alpha-2b Interferon + Dexamethasone for Incomplete or Non-Responders (LTC W. Lane)

START DATE: 1986

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Ray O. Lundy

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Multiple myeloma, Chemotherapy, Interferon

Study Objective: To compare the effectiveness of three chemotherapy induction schedules for the induction of remission in previously untreated patients with multiple myeloma. The three schedules are:

- 1) VMCP/VBAP;
- 2) VAD (a four day infusion schedule);
- 3) VMCP/VBAPP,

To compare the value of Intron-A (alpha-2b interferon) maintenance versus no maintenance for patients proven to achieve remission (at least 75% tumor regression after induction).

For patients who achieve only improvement (50-74% tumor regression) or are non-responders with chemotherapy induction, to determine whether dexamethasone plus alpha-2b Interferon (INTRON-A) will increase the remission rate and survival duration.

To determine prognostic applicability to multiple myeloma of serum beta-2 microglobulin level, plasma cell LI%, using the BU-1 monoclonal antibody, bone marrow plasma cell morphologic characteristics, and histochemical staining for acid phosphatase and beta-glucuronidase content.

Nationwide, the study group desires to accrue 450 evaluable patients in the induction phase of approximately 3.3 years, and expects to have 130 patients in the maintenance phase, and 230 patients in the dexamethasone plus interferon trial. We expect no more than 20 patients will be enrolled at WBAMC.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in Department of Clinical Investigation and are available upon request.

Progress: There have been no patients entered into this study at WBAMC. Enrollment was closed in Oct 90.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/54

STATUS: Ongoing

TITLE: Prospective Evaluation of Coccidioidomycosis in Human Immunodeficiency Virus-Infected Individuals Living in an Endemic Area

START DATE: Aug 91

ESTIMATED COMPLETION DATE: Aug 96

PRINCIPAL INVESTIGATOR: Lynn McNicol

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Naomi Aronson, MC; PA Gregory Martin

KEY WORDS: Coccidioidomycosis

Study Objective: To demonstrate whether coccidiomycosis seen in HIV patients is reactivation disease or represents acute infection in an immunocompromised host. To assess the early predictive value for active coccidioidomycosis of the spherulin skin test, coccidioides complement fixation and immunodiffusion antibody studies and coccidioides antigen ELISA in the HIV infected population.

Technical Approach: This is a prospective descriptive study. Subjects will be obtained from individuals participating in the HIV natural history study 86-49 (non-active duty) and HIV infected active duty soldiers who are followed in the WBAMC Infections Disease Clinic per AR 600-110. Completion date is dependent on number of patients enrolled and severity of their immunologic compromise. Estimated study duration is 5 years.

On entry, a complete geographic history will be obtained to assess travel to Coccidioides endemic regions (West Texas, Arizona, San Joaquin Valley in California). On entry and every 6 months thereafter, delayed hypersensitivity skin testing will be performed IAW DOD HIV staging. In addition, spherulin 1:100 (Berkeley Biologics) will be included in the battery which is already usual practice in Coccidioides endemic regions. Chest radiograph will be obtained on entry and every 12 months which is current clinical practice during HIV staging. On entry and every 6 months, the following blood tests will be ordered: T cell subset by flow cytometry, quantitative immunoglobulins and SPEP, complement fixation Coccidioides antibodies (sent to Dr. Pappagianis' laboratory at UC, Davis), Coccidioidal precipitins (sent to FSH, TX), serum for coccidioidal antigen (research test) - will be frozen at -70° F initially. On entry and every 6 months, weight will be recorded. On entry and at every subsequent staging, patient will be clinically evaluated by history and physical examination to assess for presence of active coccidioidomycosis.

Progress: Study just begun. MAJ Aronson PCS'd to WRAMC in Sep. Ms. McNicol, RN, assumed PI responsibilities.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/73

STATUS: Ongoing

TITLE: Serum Gastrin and Epidermal Growth Factor Levels in Patients with Adenomatous Polyps and Carcinoma of the Colon

START DATE: Sep 89

ESTIMATED COMPLETION DATE: Unknown

PRINCIPAL INVESTIGATOR: MAJ David M. Maccini

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Edward L. Burkhalter, MC

KEY WORDS: Epidermal growth factor; Colon neoplasm

Study Objective: The purpose of this study is to determine if there is a significant elevation of the serum levels of gastrin and EGF in patients with colon carcinoma and colonic adenomatous polyps when compared to a control population (patients with a normal colonoscopy).

Technical Approach: Measurement of serum gastrin and epidermal growth factor will be performed in three groups of patients. Group one will be patients who are found to have polyps (adenomatous or hyperplastic) at colonoscopy. Group two will consist of patients who are found to have colorectal carcinoma at colonoscopy or surgery. And group three will include patients who have undergone colonoscopy and had a normal examination (no prior history of colonic polyps or cancer). Patients will be between the ages of 18 and 99 (male and female) and have no history of other malignancies or peptic ulcer disease. It is expected that most patients will be recruited prior to or after undergoing colonoscopy in the GI Clinic at WBAMC. Indications for colonoscopy will be independent of this study. Twenty patients will be included in each group.

Patients will have ten milliliters of blood drawn at the time their IV is being started for colonoscopy. This will end the patient's participation in the study. Findings at colonoscopy will be noted on the usual endoscopic record used by the clinic (WBAMC form 524). Blood will be taken to Clinical Investigation where it will be centrifuged and the serum frozen. Measurement of epidermal growth factor levels will be performed by RIA by an assay previously set up in Clinical Investigations. Gastrin levels will be processed through the Nuclear Medicine Service. Statistical analysis of the data in each group will be performed and compared. A p value <0.05 will be considered statistically significant.

Progress: Sixty serum samples were collected including a few colon carcinoma patients, as available. Setting up the assay to measure serum epidermal growth factor is causing the delay in study completion. DCI is having some difficulty obtaining a sensitive assay but work is ongoing.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 88/46

STATUS: Terminated

TITLE: Rate of Spherulin Skin Test Conversion Among Basic Trainees Exposed to Desert Training at Fort Bliss, Texas

START DATE: Sep 88

ESTIMATED COMPLETION DATE: Nov 90

PRINCIPAL INVESTIGATOR: CPT Bryan Martin

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Spherulin, Skin test to *C. immitis*.

Study Objective: To establish the rate of spherulin skin test conversion among active duty basic trainees who are exposed to desert training at Fort Bliss, Texas. To attempt to define the morbidity associated with *Coccidioides immitis* in terms of time lost from basic training due to acute *Coccidioides* infection.

Technical Approach: Basic trainees will be invited to participate in the study. Study participants will be briefed by the principal investigators about the study and given an opportunity to volunteer for the program. One basic training cycle will be tested in each month to determine if there is a seasonal peak to exposure. As basic training cycles are 8 weeks in length and encompass between 60-240 soldiers (average 180) and begin every week, except the 2 weeks prior to Christmas, 12 basic training cycles will be studied, giving an approximate total study base of 2,400 soldiers in 1 year. This has been coordinated with the S-3 (plans) of the Training Brigade.

Each participant will fill out a preformatted questionnaire which will identify each volunteer by name, age, sex and provide a brief history of areas where the participant has lived prior to basic training and the number of years he has lived in each area. This will enable the investigators to provide a *C. immitis* exposure index which will categorize each soldier as having a low, medium or high index of exposure. In a large group of people with an infinite degree of exposure this will provide relevant criteria to judge each participant's risk of prior exposure. This questionnaire will also be used to chart sensitivities and other relevant information. These will be filled in by the soldier and returned to the investigators and kept on file.

Based on the information received in this questionnaire, each participant will be assigned to a group with a low, medium, or high exposure to *C. immitis*. This grouping will be based on the historical data given by the patient concerning where he lived and amount of time spent in each state. The states have been divided into 3 groups and given a statistical score based on the expected rate of exposure to *C. immitis* based on epidemiologic studies of the regions with endemic *C. immitis*.

Each state is assigned a value:

a.2 for high possibility of exposure to *C. immitis*

(1) California

(2) Arizona

(3) New Mexico

b.1 for moderate possibility of exposure to *C. immitis*

(1) Texas

(2) Utah

(3) Nevada

c. 0 for low probability of exposure to *C. immitis*; this includes all other states.

Each participant is assigned a sum product of (State's assigned value) X (number of years lived in the state). The sum value is used to determine the life exposure index.

a. Low: 1-10

b. Moderate: 11-25

c. High: 26+

The life exposure index will then be correlated with the statistical rate of skin test positivity among our tested population.

Each participant will be skin tested to spherulin. 0.1ml of antigen will be injected intradermally after cleaning the area with 70% alcohol. Patients will be observed for 20 minutes after the test placement to record any positive immediate reactions. The reaction size will then be measured at approximately 48-72 hours after placement. Induration of 5mm or greater will be considered a positive reaction. Those who react to this first test, indicating previous sensitivity, will be included in the study for statistical purposes only. They will not be further tested. Tetanus will be used as a control antigen to ensure the patient is not anergic. The identity of those soldiers who are skin test negative to both tetanus and spherulin will be recorded for appropriate follow-up; it is estimated that as many as 40% of patients will not react to either spherulin or to tetanus.

These same soldiers (only those who did not react to spherulin on the first testing will be retested with spherulin within 1 week of graduation from basic training, using the same technique as listed above. The results will be tabulated for statistical analysis. We will ascertain the location of AIT training for all participants who remain skin test negative and if they remain in El Paso, they will be re-enrolled in an extended study and followed with repeat skin testing at the end of their 7 weeks of Advanced Individual Training (AIT), giving a total study time of 15 weeks. Also during the repeat testing, those subjects listed above who did not initially react to either tetanus or to spherulin will further receive an anergy test utilizing a battery of injections to test for skin test reactivity to tetanus, mumps, monilia and trichophyton. Those who do not react to any of these antigens will be considered anergic and will be consulted to the Allergy Clinic for any further workup required. We estimate less than 5 percent of our subjects will fall into this classification. The results of testing on any subject who meets this definition of anergy will not be included in the data base for this study.

AMENDMENT: Each participant will be skin tested to spherulin. 0.1ml of antigen will be injected intradermally after cleaning the area with 70% alcohol. Patients will be observed for 20 minutes after the test placement to record any positive immediate reactions. The reaction size will then be measured at 24, 48 and 72 hours after placement. Induration of 5mm or greater will be considered a positive reaction. Those who react to this first test, indicating previous sensitivity will be included in the study for statistical purpose only. They will not be further tested with spherulin. Those who are skin test positive at 24 hours, but negative at 48 hours will be considered to be negative for the purposes of this study, and will be retested at the end of basic; in addition, they may have blood drawn for lymphoblast activity studies, in order to look at the possibility of false positive reactions in this group. Blood will also be drawn from representative soldiers who are skin test positive at 48 hours and who are skin test negative in order to validate and standardize the lymphoblast activity assay.

Progress: This protocol was terminated due to PCS of the investigators.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/03

STATUS: Terminated

TITLE: Malignancy Associated Changes in Peripheral Blood Smears

START DATE: Oct 89

ESTIMATED COMPLETION DATE: Jun 90

PRINCIPAL INVESTIGATOR: CPT Bryan Martin

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ I.L. Levey, MC

KEY WORDS: Cancer; blood cells

Study Objective: Analyze leukocytes from patients with non-hematologic cancer searching for patterns of cellular structure identifiable with the light microscope and indicative of underlying malignancy.

Technical Approach: Each individual will fill out a basic data sheet listing past medical history, past surgical history, past and present medications, and allergies. A known diagnosis of malignancy will be noted with histologic type and clinical stage if possible.

Three smears will be obtained from capillary blood of each patient along with 7cc of blood collected from the antecubital vein from which 3 smears will be made. The cytomorphological features described by Johnston et al. were noted in smears from earlobe blood and finger tip blood. To confirm their findings and determine if these features can also be found in the antecubital vein blood, both sources will be collected from patients with known malignancy. If early results indicate there is a good correlation between antecubital vein blood and fingerstick or ear lobe capillary blood, then only venous antecubital blood will be used, as this is the method of routine collection and judged less painful than fingertip collection.

Smears will be stained and examined as follows: blood will be collected four hours after meals, preferable in the morning to control possible variables in a similar method as Johnston et al. There should be no surgery or transfusion of blood 2 months prior to the test. Fingertip and ear lobe blood will be obtained by scrubbing the area with 70% alcohol which is allowed to dry. Blood will be expressed with lancet and small drop placed on a slide. This smear will be prepared by either mechanical smear maker or manual "spreader slide" technique. The slides will be allowed to air dry for 5-10 minutes and fixed with anhydrous acetone free methanol for 30 minutes.

Smears will be stained with a modified Wright-Giemsa stain as per Johnston et al: Undiluted Wright's for 3 minutes, then Wright's diluted with equal amount of distilled water for 3 minutes. the slide will then be rinsed with water and stained with 1:10 diluted Giemsa for 13 minutes followed by water rinse and air dry.

The smears will be examined with the 100x oil immersion objective of a Zeiss photomicroscope III. A standard manual differential count will be performed on each specimen and representative photomicrographs will be taken. The leukocytes will be examined for two hematologic parameters: (1) the polymorphonuclear leukocytes will be inspected for the presence of excrescences, which are thread-like, thin, non-pedunculated projections from the nucleus, and the percent with excrescences will be calculated, (2) the cytoplasm of large mononuclear cells will be examined for the presence of small inclusion bodies surrounded by lightly stained areas or halos. One hundred mononuclear cells will be examined to estimate the percent haloed bodies.

Progress: This protocol was terminated due to PCS of all investigators.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/78

STATUS: Terminated

TITLE: Food Sensitivity and Inhalant Allergy: Effect of Immunotherapy

START DATE: Sep 89

ESTIMATED COMPLETION DATE: Aug 90

PRINCIPAL INVESTIGATOR: LTC David L. Michaels

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Allergy, Food sensitivity, Immunotherapy

Study Objective: This project will investigate the incidence of allergy to various foods in patients being treated for inhalant allergy. Change in reported food allergy symptoms following inhalant immunotherapy will be investigated to determine whether the food symptoms represent cross reactivity with IgE antibody to inhalant allergens.

Technical Approach: The first phase of this study will employ a questionnaire to evaluate the frequency of adverse reactions to various ingestants including foods, preservatives, food colors, alcohol, and aspirin. This questionnaire will be distributed to all patients currently being treated with immunotherapy at WBAMC Allergy Clinic. Patients who agree to participate in the study will also be queried whether any of the ingestant symptoms have changed following inhalant immunotherapy. responses will be correlated with skin test results, antigens contained in immunotherapy mix, and duration of immunotherapy.

Where possible correlations between food and inhalant allergen are found, repeat skin testing with both antigens will be performed using the skin prick test titration method to measure degree of sensitivity. RAST assays will also be performed to highly reactive foods to determine correlation with skin prick test results. Selected patients may also be asked to participate in double blind food challenges to confirm the relationship of food ingestion to symptoms. A second phase of this study will use information obtained from the questionnaire. New patients being evaluated for inhalant allergy at WBAMC Allergy Clinic will be questioned about possible food sensitivities. Skin prick tests to the most commonly implicated foods will routinely be done in patients having positive skin tests to inhalant allergens. The food skin test results will be compared with the pattern of inhalant skin test reactivity and the presence of symptoms recorded on the history form. Testing of 200 patients in this manner should determine whether a particular positive food skin test in an inhalant sensitive person is of any clinical significance or merely represents antibody cross reactivity.

Progress: Project terminated. Tabulation of 210 questionnaires failed to reveal significant incidence of good and inhalant cross-reactive allergy. This is likely due to the local environment lacking pollens previously incriminated in causing the oral allergy syndrome (e.g., Birch, ragweed). Some patients were approached concerning documentaiton of food allergy by testing and/or challenge, but they did not choose to participate.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/03

STATUS: Ongoing

TITLE: Learning and Behavior Disorders in Children Referred for Allergy Evaluation

START DATE: Nov 89

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: LTC David L. Michaels

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: A.W. Atkinson, LTC, MC

KEY WORDS: Attention-deficit disorder, Behavior, Allergy

Study Objective: This project will use a questionnaire to assess the frequency and type of learning and/or behavior disorders in children age 5-12 who are referred to the Allergy Clinic for evaluation of presumed allergic respiratory symptoms (rhinitis, asthma).

Technical Approach: Parents of 100 successive children from age 5-12 being referred for allergy evaluation will be asked to complete the Yale Children's Inventory Questionnaire. These will be reviewed and scored by staff of the Developmental Pediatric Service. If significant abnormalities are identified, parents will be contacted and appropriate interventions will be instituted if deemed necessary by the Developmental Pediatrician.

All children with diagnosed allergy will be prescribed customary allergy treatment to include medications, allergen avoidance, and possibly immunotherapy.

One year after the initial evaluation, each child will be recalled for allergy follow-up. The Yale Inventory will be repeated and scores will be compared with those before allergy treatment. Patterns of significant change in specific areas of learning or behavior may indicate beneficial effects from allergy treatment in children with specific problems.

There are no additional risks to subjects who participate in this study. The usual allergy testing and treatment will be carried out as for patients not in the study. The only additional procedure is the completion of the questionnaire.

Progress: Fifty patients entered the study. Preliminary examination of data indicated a tendency toward increase attentional disorders in allergic children. This was submitted in abstract form to the American College of Allergists meeting but was not accepted for presentation. No further data have been collected since, but PI will continue as time permits.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 86/34

STATUS: Ongoing

TITLE: The Effects of Verapamil and Diltiazem on Gastric Emptying

START DATE: Dec 87

ESTIMATED COMPLETION DATE: Jun 92

PRINCIPAL INVESTIGATOR: MAJ Albert J. Moreno

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Morakinyo A. Oyewole Toney

KEY WORDS: Gastric Emptying, Calcium channel blockers

Study Objective: Calcium channel blockers are currently indicated in the treatment of several medical problems. Data on the effects of calcium channel blockers on gastric emptying currently is sparse, but potentially important. This study is to determine the effects of verapamil and diltiazem on gastric emptying in normal human volunteers.

Technical Approach: Selection of patients: Twenty healthy (10 male, 10 female) nonpregnant volunteers with an age range of 21-40 will be studied. Patients with any underlying medical problem, on any medication, with a known allergy history to verapamil or diltiazem, or with an abnormal gastric emptying study will be excluded from the study. Patients will also need a normal physical examination, vital signs, EKG, and SMA-20 prior to entering the study. A BHCG will be drawn on all female patients.

Radiation doses: Each patient will have three studies. Each study consists of 1 mCi Tc-99m SCOL and 250 uCi of In-111 DTPA. The target organs for the Tc-99m SCOL and the In-111 DTPA will be the stomach and colon. The stomach may receive approximately 340 m/rad from Tc-99m SCOL. The distal bowel may receive up to 650 m/rads from the In-111 DTPA. These are acceptable levels of radiation exposure.

Patients presenting to the Gastroenterology Service, WBAMC, will be invited to participate in the study. They will be assigned a number for identification purposes. Each subject will undergo study with each drug. A daily history and physical exam will be accomplished.

Gastric emptying: A modification of the technique prepared by Heading et al. will be used. Both solid and liquid phases will be studied. The solid phase will be a standard meal of beef stew impregnated with 1 mCi of 99mTechnetium labeled sulfur colloid. The liquid phase will be 150cc of water combined with 250 uCi of 111Indium labeled diethylene-triamine-pentaacetic acid 111In-DTPA). The time of ingestion of the meal is defined as the midpoint in the period of ingestion. Initial scanning is done every 15 minutes (60 sec images) for a total of three hours. During scanning the patient will be supine, but at all other times they will be seated in a chair.

Methods: Baseline scan: Day 1. If this is abnormal (40% retention at three hours), the patient will be excluded.

Scan 2: Patients on verapamil for three days or diltiazem for one dose. Last dose of the medication will be 30 minutes prior to scanning. The patient will have nothing by mouth after midnight except for medications. The patients will be randomized to receive verapamil or diltiazem first. There will be a one-week minimum of time off the initial medication prior to starting the second medication. A plasma concentration of the drug will be drawn prior to the gastric emptying study.

Scan 3: The patient will receive the second drug in the same format. The patient will be examined daily by an associate investigator during the investigational period.

Statistical analysis: Student t-test

Medications: Verapamil: Dosage schedule will be 80mg by mouth every six hours. The mean elimination half-life in single dose studies ranged from 2.8 to 7.4 hours. After continuous dosing (every six hours for ten doses) the half life increases to 4.5 to 12.0 hours. Therefore, the drug will be administered for three days prior

doses) the half life increases to 4.5 to 12.0 hours. Therefore, the drug will be administered for three days prior to testing. The last dose will be 30 minutes prior to testing.

Potential side effects: Cardiovascular: Hypotension - 2.9%, peripheral edema - 1.7%, AV block - 0.8%, bradycardia - 1.1%, CHF or pulmonary edema - 0.9%; Central nervous system: Dizziness - 3.6%, headache - 1.8%, fatigue - 1.1%; Gastrointestinal: Constipation - 6.3%, nausea - 1.6%.

Side-effects with less than 0.5% incidence and where a causal relationship is not certain: confusion, paresthesia, insomnia, somnolence, equilibrium disorders, blurred vision, syncope, muscle cramps, shakiness, claudication, hair loss, macular eruptions and spotty menstruation.

Diltiazem: Dosage schedule will be 60mg by mouth 30 minutes prior to the test. The plasma elimination half life is 3.5 hours whether single or multiple administrations are used; therefore, a single dose is sufficient.

Progress: Four subjects were enrolled. Due to personnel and equipment restraints, this protocol has not been given its due priority. Currently, the senior nuclear medicine fellow will be following up on this protocol and study should be completed in eight months.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/51

STATUS: Completed

TITLE: Emergency Use of 131I MIBG (IND #17,239) in a Patient L.R.

START DATE: Jul 91

ESTIMATED COMPLETION DATE: Jul 91

PRINCIPAL INVESTIGATOR: LTC Albert J. Moreno

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Adrenal medullary scan

Study Objective: HSC approved one-time emergency use of 131I MIBG for diagnostic visualization of small adrenal/extra-adrenal tumors with nuclear medicine imaging devices. Patient had persistent elevation VHA/catecholamines and metanephrines which may suggest paragangliomas.

Technical Approach: Patient will be injected intravenously with the radiopharmaceutical. Images will be obtained at 48 hours post injection. Images may also be obtained at 24 and 72 hours post injection.

Progress: The adrenal medullary study was successfully completed on patient without any adverse effects. The proper radiopharmaceutical dose and imaging techniques were employed and the study was negative for metastatic pheochromocytoma.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/60

STATUS: Ongoing

TITLE: Emergency Use of VM-26 in Patient with Lymphoblastic Lymphoma, IV_B, High Risk

START DATE: Aug 91

ESTIMATED COMPLETION DATE: Dec 91

PRINCIPAL INVESTIGATOR: MAJ Michael E Nash

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Lymphoma, Lymphoblastic, VM-26

Study Objective: VM-26 is needed as part of consolidation therapy for 22 y/o male patient with high grade LBL.

Technical Approach: Drug will be obtained from NCI and will be administered in accordance with accompanying instructions.

Progress: Patient has received VM-26 per protocol outline. No adverse effects noted to date. Therapy is ongoing.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 88/74

STATUS: Ongoing

TITLE: Echocardiographic Standards for Adolescents Based on Tanner Staging

START DATE: Aug 88

ESTIMATED COMPLETION DATE: Jun 91

PRINCIPAL INVESTIGATOR: COL William Pearl

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Dr. Martinko, Dr. Stafford, Dept of Pediatrics

KEY WORDS: Echocardiography, Puberty

Study Objective: To establish echocardiographic standard for healthy adolescents based on Tanner staging, which measures biologic age rather than chronologic age. The new standards will allow a more narrow definition of normal.

Technical Approach: We propose to obtain an echocardiogram on consenting patients presenting to the Pediatric and Adolescent Clinic for school or sport physicals, between 10 and 17 years of age. Tanner staging will be assessed by examiners, which is part of the normal physical examination. Complete physical examinations will be performed and subjects with evidence of chronic illness or heart or lung disease will be excluded. Furthermore, a questionnaire is to be completed by each subject which elicits additional information on athletic activities and health. The patient will be sent to the Cardiology Clinic upon completion of the physical examination for an echocardiogram to be performed by a trained technician.

Echocardiographic data will be measured by computer analysis and reviewed by a pediatric cardiologist. Measurements will include the thickness of the right free ventricular wall, interventricular septum, left ventricular free wall, aortic root, left atrium, aortic valve opening, and each of the identifiable portions of the mitral valve motion. From the data collected, mean values and standard deviations will be determined for males and females in each of the five Tanner stages. Additional data to be collected on each subject will include height, weight, race, and body surface area.

Progress: M-mode echocardiograms were recorded from 298 healthy adolescents between 10 and 16 years of age. Nineteen measured and ten calculated parameters were correlated with subjects' gender and sexual maturity rating. Significant ($p < .05$) differences by gender were demonstrated for 21 of 29 parameters. Sexual maturity rating had a significant effect on 4 of 29 parameters for boys and on 5 of 29 parameters for girls, when controlling for body surface area. Fourteen of 29 parameters in boys and 3 of 29 parameters in girls showed a significant effect of sexual maturity rating when controlling for age. The male adolescent growth spurt in lean body mass is paralleled by a similar growth spurt in left ventricular volume. Publication of final paper is pending.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/64

STATUS: Ongoing

TITLE: RV 26, Tri-Service HIV Biopsychosocial Study

START DATE: Sep 91

ESTIMATED COMPLETION DATE: Mar 92

PRINCIPAL INVESTIGATOR: Beverly Simm

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Connie Jensen-Wilczewski

KEY WORDS: HIV

Study Objective:

a. To consolidate psychosocial data in HIV-infected military medical beneficiaries in a form which lends itself to analysis. This information will be of practical and scientific value for individual participating medical centers, each military service, and the Department of Defense.

b. To develop analogous databases at tri-service study sites that use identical measures.

c. To identify and refine useful clinical measures that can be used to predict HIV exposure or transmission risk and risk for psychosocial morbidity.

d. To develop, pilot and validate a new instrument and methodology that relates HIV and other STD risk behavior data and HIV transmission risk. Such information will be anonymous until and unless sufficient confidentiality guarantees are available to allow for linked data collection.

e. Develop databases for the following biopsychosocial study areas:

- psychosocial factors associated with HIV transmission risk behaviors.
- areas of focus for psychiatric and psychosocial interventions most likely to significantly impact on the spread of infection.
- evaluation of the role of psychosocial phenomena such as social supports and methods of coping in reducing HIV transmission and HIV-related morbidity in HIV-infected persons.
- areas of focus for biopsychosocial interventions most likely to prevent neuropsychiatric progress of HIV disease and limit its consequences in seropositives.
- baseline rates of salient phenomena in seronegatives.
- evaluation of effectiveness of HIV transmission reduction interventions by using measures from this study as pre-intervention baseline and post-intervention outcome measures.

Technical Approach: All HIV-infected military medical beneficiaries followed by the WBAMC Infectious Disease Service are eligible for inclusion in this protocol. Anticipated enrollment for the 6-month period is 30. The study will be explained verbally and in written form to potential eligible subjects. Consenting subjects will be asked to sign a volunteer consent form. The Anonymous Behavior Survey will be administered by the investigators who are Infectious Disease Service HIV Social Workers. In order to maintain a participant's anonymity, there will be no identifying information collected with the survey. Participants will complete the survey either alone or in a group of no more than 5 people (adequate space will be provided to maintain privacy). The surveys will be collected in a locked box and be sent to the Henry M. Jackson Foundation for data interpretation. Results will be reported only for all information combined across all completed survey, not individuals.

Progress: Study just approved. Volunteer recruitment is underway.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 86/49

STATUS: Ongoing

TITLE: The Natural History of HTLV-III Infection and Disease in a US Military Population

START DATE: May 86

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ David Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Charles E. Davis, Jr., MAJ Eugene Etzkorn; PA Gregory E. Martin; MAJ Wellington Sun, MC; Ms. Lynn B. McNicol, RN

KEY WORDS: HIV Natural History

Study Objective: Study the epidemiology of HTLV-III infection in active duty and retired military personnel and their dependents.

Technical Approach: Standard evaluation will be routine medical evaluation, immunological evaluation, laboratory tests, tests for opportunistic infections, HTLV-III viral cultures on body fluids and organs whenever possible. Completion of HTLV-III clinical evaluation form. HTLV-III tests. Counselling, education, and referral of contacts. Follow-up of individuals in the study. Data analysis: disease progression will be studied, as defined by Walter Reed Staging Classification. The effect of variables, including but not limited to age, sex, ethnic background, risk factors, length of infection, and simultaneous viral infections, will be studied.

Addendum: 12 Feb 90 - This protocol was amended to exclude active duty servicemembers. At the directive of the Secretary of the Army, all active duty HIV+ servicemembers are to be clinically staged periodically.

Progress: This protocol is part of an Army-wide study; all WBAMC data is submitted to a central data base at WRAIR. It is impossible to analyze our local data in terms of progress, but we provide it to USADHS who recently submitted for publication the trends of DOD/US Army HIV protocol.

186 subjects were entered. 101 patients were lost to followup for the purposes of this study (17 died; 25 location unknown due to PCS, TDRL, Chapter actions, deportation; 59 PCS'd to other posts and are followed at other medical centers. WBAMC is currently following 75 patients in various stages as indicated below. Status of patients: 23 active duty, 22 medical retired, 10 VAB, 13 dependents, 7 other (Bureau of Prisons, Immigration Service, Indian Health Service).

WR1WR2WR3WR4WR5WR6Staging

6 23 24 412 4 (AIDS) 6

MAJ Aronson PCS'd in Sep and MAJ Slagle assumed PI responsibilities.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/22

STATUS: Ongoing

TITLE: Prospective Evaluation of Health Care Workers Exposed to the Blood of Human Immunodeficiency Virus (HIV)

START DATE: Mar 89

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ David Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Wellington Sun, MC; Ms. Lynn McNicol, RN; Ms. Renata Riley, PA-C

KEY WORDS: HIV, occupational exposure

Study Objective: The objectives of this prospective surveillance project are:

- 1) To estimate the risk of HIV infection in health care workers (HCWs) exposed via the parenteral or mucous membrane route to HIV infected blood, according to type of exposure.
- 2) Describe infection control precautions taken or not-taken to evaluate extent of preventable exposures.
- 3) To describe the clinical natural history and development of laboratory markers of HIV infection in health care workers enrolled in this project who seroconvert to HIV.

Technical Approach: The number of exposed health care workers is expected to be less than 30/year, but is dependent on the number of HIV infected individuals cared for at WBAMC, a population which is increasing in size.

Upon entry into the surveillance project, each exposed HCW will be interviewed and a questionnaire completed collecting the following data: demographic information, use of immunosuppressive drugs, circumstances of the blood exposure, type of infection control precautions used at the time of exposure, any past exposure prophylaxis and information on the source patient. The exposed HCW will be asked to complete a questionnaire concerning risk factors for HIV infection. This confidential report will be completed by the exposed HCW and mailed directly to CDC by the worker. Information collected on this form (CDC 57.42A) will not be released to personnel at WBAMC.

The exposed HCW will be prospectively followed by the investigators for one year with follow up data and specimen collection at 6 weeks, 3 months, 6 months, and one year post exposure. At each follow-up a questionnaire and 10 ml. serum will be sent to CDC. In addition to scheduled follow-ups the exposed HCW must report to the investigator any illness of at least one week duration which occurs in the 12 week period after exposure. If the symptoms are suggestive of an acute retroviral syndrome, the investigator will obtain whole blood for virus isolation +T cell subset (10 ml) and serum (10 ml) for antibody/antigen testing.

Baseline serum samples will be tested for HIV antibody, if negative, HIV antigen will also be evaluated. If a HCW seroconverts a 10 ml heparinized whole blood sample will be requested from the source patient with their informed consent. Viral isolates from the source patient and HCW will be compared using molecular techniques.

Exposed health care workers will be followed for one year post-exposure.

Progress: Of the 7 individuals entered in this study, 5 are needlestick injuries, 2 blood to non-intact skin exposure. 2 individuals initiated zidovudine post exposure therapy (WBAMC protocol #89/67). No seroconversions were found. MAJ Aronson PSC'd in Sep and MAJ Slagle assumed PI responsibilities.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/66

STATUS: Ongoing

TITLE: Use of Itraconazole for Treatment of Coccidiomycosis (Monitor: COL Cannady)

START DATE: Jan 89

ESTIMATED COMPLETION DATE: Sep 91

PRINCIPAL INVESTIGATOR: MAJ David C. Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Wellington Sun, MC

KEY WORDS: Itraconazole, Coccidiomycosis

Study Objectives: To assess the efficacy of Itraconazole therapy in fungal disease. The study is a non-blinded, non-crossover study to assess drug efficacy. Medication used will be Itraconazole. Population studies will be those with fungal disease who have failed on standard drug therapy.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: MAJ Slagle assumed PI responsibilities 1 Sep due to MAJ Aronson's PCS. Patient with chronic pulmonary cocci has had good therapeutic response with CF titers 1:256→1:8, negative cultures and nor further sweats, fevers, hemoptysis. Patient with renal failure and cocci osteomyelitis/arthritis improved; can ambulate without pain and has had cocci CF titers 1:64→1:16. Both suggestive of clinical response.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/67

STATUS: Ongoing

TITLE: Investigational Prophylactic Use of Zidovudine in Health Care Workers Sustaining a Deep Percutaneous Occupational Exposure to Human Immunodeficiency Virus (Monitor: COL Cannady)

START DATE: Jul 89

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ David C. Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Ms. Lynn B. McNicol, RN; Ms. Renata Riley, PA-C; MAJ Wellington Sun, MC

KEY WORDS: Zidovudine, Occupational HIV

Study Objective: To offer a defined course of zidovudine to HIV negative health care workers within 5 days of a significant exposure to HIV. To assess the safety and tolerance of 200mg zidovudine given orally every 6 hours for 42 days in otherwise healthy persons.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: MAJ Slagle assumed PI responsibilities on 1 Sep due to MAJ Aronson's PCS. Two individuals with needlesticks involving HIV infected blood on the needle elected to take zidovudine. One completed 42-day course and is seronegative at 6-month followup. The other individual commenced therapy in mid August. One individual on zidovudine experienced nausea, anorexia, headache and insomnia, but remains on therapy at time of this report.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/84

STATUS: Terminated

TITLE: Induction of Tumor Necrosis Factor Alpha (TNF-alpha) in Human Infection with Coccidioides immitis

START DATE: Oct 89

ESTIMATED COMPLETION DATE: Oct 91

PRINCIPAL INVESTIGATOR: MAJ David C. Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Matthew J. Dolan, MC, USAF; Rebecca A. Cox, Ph.D.; MAJ J. William Kelly, MC; MAJ Robert A. Zajac, MC, USAF; MAJ Gregory P. Melcher, MC, USAF

KEY WORDS: Coccidioides immitis, Tumor necrosis factor alpha

Study Objective: To determine if human infection with the dimorphic fungus Coccidioides immitis induces the production of cytokine TNF-alpha/cachectin as part of the overall host immunologic response to infection.

Technical Approach: Patients and controls (staff volunteers) from each facility will be phlebotomized on one occasion; approximately 50 ml of blood by peripheral venipuncture will be required. Antigen stimulation will be performed at WBAMC by MAJ Slagle, using the facilities of the Department of Clinical Investigation. Supernatants from this portion of the assay will be frozen at -70°C, batched and transported at a future date to the San Antonio State Chest Hospital (SASCH). The TNF-alpha RIA will be performed by the Research Immunology Laboratory at SASCH.

Patients suitable for inclusion in this study include individuals 18 years of age or old or older having documented active infection with C. immitis, as evidenced by:

1. Acute pneumonitis with positive sputum culture.
2. Disseminated disease within the thorax, with pulmonary parenchymal involvement as shown by biopsy stain or culture.
3. Extrathoracic disseminated disease, with demonstration of C. immitis on biopsy stain or culture of involved tissue or biologic fluid.

Exclusion criteria for patients and controls include the presence of concurrent infection or underlying malignancy. Patient controls will be matched for age (\pm 10 years), sex, and race.

Risks to patients and controls are limited to those risks associated with phlebotomy (bruising, infection, or thrombophlebitis at the venipuncture site). The study is designed to begin in October 1989 upon IRB approval, with an anticipated duration of two years. It is anticipated that 5-10 patients from WBAMC will be eligible for enrollment in each year of the study.

PBM from each patient and control will be stimulated in vivo with Formalin-killed spheres (test antigen), lipopolysaccharide (LPS) from E. coli serotype 055:B5 (positive control), and tissue culture media (negative control). thus, TNF-alpha levels will be analyzed using two-factor analysis of variance (factors of infected/not infected and stimulated/not stimulated).

Progress: Project terminated with no patients entered. Other clinical and research obligations preclude the PI from continuing the study.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/05

STATUS: Ongoing

TITLE: A Treatment IND Protocol for the Use of 2'3'-dideoxyinosine (ddI) in Patients with AIDS or ARC Who Are Intolerant to Zidovudine (Monitor: COL Cannady)

START DATE: Dec 89

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ David Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Ms. Renata Riley, PA-C; Ms. Lynn B. McNicol, RN

KEY WORDS: Dideoxyinosine

Study Objective: To make ddI available to persons with HIV infection who have developed intolerance to Zidovudine (AZT) and to evaluate the toxicity of ddI in AIDS/ARC patients.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: MAJ Slagle assumed PI responsibility when MAJ Aronson PCS'd. Six patients intolerant to zidovudine have been entered in this protocol. One died (not due to drug); one developed the side effect of severe pancreatitis necessitating termination of therapy; one developed an ileus and diarrhea (to include on rechallenge) and elected to withdraw; one developed dementia and hemodialysis dependency and was withdrawn from protocol.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/54

STATUS: Ongoing

TITLE: Efficacy of Passive Immunization in the Prevention of Infection Due to Klebsiella pneumoniae and Pseudomonas aeruginosa

START DATE: Oct 90

ESTIMATED COMPLETION DATE: Sep 93

PRINCIPAL INVESTIGATOR: MAJ David C. Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Naomi Aronson, MC

KEY WORDS: IVIG, passive immunization, Klebsiella pneumoniae, Pseudomonas aeruginosa

Study Objective: (1) To determine the efficacy of intravenous immunoglobulin (IVIG) compared with albumin in reducing the incidence of infection caused by Klebsiella and Pseudomonas bacterial serotypes contained in the two vaccines. (2) To determine whether IVIG delays onset or lessens severity of serotype-specific infection.

Technical Approach: In a double blind, randomized fashion, study participants will receive a one time IV infusion of K-P IVIG (5gms, 7gms, 9gms, or 11gms depending on weight of $\leq 50\text{Kg}$, $51-70\text{Kg}$, or $\geq 91\text{Kg}$, respectively) and multivitamins or albumin and multivitamins. All patients will be followed daily for signs of infection while in the hospital for a maximum of 6 weeks. Patients who are discharged prior to this time will be telephoned to ascertain 6-week survival status.

Amendment: Amended infusion time range to 45-90 minutes on the consent form.

Progress: Only fifteen patients have been enrolled, which is less than expected (20/month are needed). An unexpectedly large number of patients have declined to participate. PI will endeavor to improve patient education to increase participation rate. Problems have been encountered in the saving of clinical isolates and shipping of same in the Microbiology Lab (specimens referred to WRAIR). Problems will be discussed with MAJ Gelston (new Micro Chief). Only one position (nurse clinician) has been hired thus far, but given low enrollment numbers, on full time employee is sufficient at present.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/23E

STATUS: Ongoing

TITLE: Emergency Use of Itraconazole for Treatment of Sporotrichosis (Patient F.L.)

START DATE: Apr 91

ESTIMATED COMPLETION DATE: Indef

PRINCIPAL INVESTIGATOR: MAJ David Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Sporotrichosis, Itraconazole

Study Objective: Emergency one-time approval sought to treat patient with progressive skin lesions and fever despite amphotericin B who is developing renal insufficiency (creatinine 4.2) in an effort to preserve the patient's life and renal function.

Technical Approach: Itraconazole will be used in accordance with Janssen single patient protocol (JRD 51,211/CC), IND 24,313).

Progress: Patient has disseminated sporotrichosis (blood, skin, lung, right knee) and developed renal failure on Ampho B. He was subsequently changed to Itraconazole and showed improvement of infection except for persistent right knee/erosion of medial femoral condyle. Positive gallium in area suggesting progression, change due to infection which may require surgical management. Patient is fairly asymptomatic in knee and resistant to invasive procedures. No side effects are noted with Itraconazole in this patient. MAJ Slagle assumed PI responsibilities due to MAJ Aronson's PCS.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/23

STATUS: Ongoing

TITLE: Use of Itraconazole for Treatment of Sporotrichosis (Monitor: COL Cannady)

START DATE: Apr 91

ESTIMATED COMPLETION DATE: Indef

PRINCIPAL INVESTIGATOR: MAJ David C. Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Wellington Sun, MC

KEY WORDS: Sporotrichosis, Itraconazole

Study Objective: To assess the efficacy of itraconazole in sporotrichosis in a non-blinded, non-crossover study under the Janssen Pharmaceuticals' protocol (IND 24,313) on patients who have failed available standard therapy (e.g., amphotericin B, ketoconazole) due to lack of efficacy, adverse effects or contraindications for use.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: MAJ Slagle assumed PI responsibilities 1 Sep due to MAJ Aronson's PCS. One patient is enrolled who has disseminated sporotrichosis (blood, skin, lung, right knee) and developed renal failure on Ampho B. He was subsequently changed to Itraconazole and showed improvement of infection except for persistent right knee/erosion of medial femoral condyle. Positive gallium in area suggesting progression, change due to infection which may require surgical management. Patient is fairly asymptomatic in knee and resistant to invasive procedures. No side effects are noted with Itraconazole in this patient.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/50

STATUS: Ongoing

TITLE: An Open Label Regimen of Videx (2'3'-dideoxyinosine, ddI) in Children with Acquired Immune Deficiency Syndrome (AIDS) Who Have Demonstrated Significant Deterioration or Intolerance to Zidovudine (Retrovir)(Monitor: MAJ Wellington Sun)

START DATE: Oct 91

ESTIMATED COMPLETION DATE: Undetermined

PRINCIPAL INVESTIGATOR: MAJ David C. Slagle

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Martin Weisse, MC

KEY WORDS: AIDS, Videx

Study Objective: This open compassionate use protocol is to provide an investigational new antiretroviral agent, 2'3'-dideoxyinosine (ddI), to children with advanced HIV infection who are unable to take zidovudine (Retrovir). Patients will be closely monitored during the course of this protocol to assess drug efficacy and to monitor for signs of drug toxicity or adverse reactions.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Study approved by WBAMC IRB and forwarded to HSC for further approval in Sep.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/06

STATUS: Ongoing

TITLE: A Prospective Double-Blind Study of Retrovir in the Treatment of Patients with Early HIV-Associated Immunodeficiency (Monitor: COL Cannady)

START DATE: Dec 88

ESTIMATED COMPLETION DATE: Sep 91

PRINCIPAL INVESTIGATOR: MAJ Wellington Sun

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Shannon M. Harrison (FAMC), MAJ David C. Slagle (WBAMC)

KEY WORDS: Zidovudine in Early HIV

Study Objective:

1. To evaluate the safety and tolerance of chronic administration of RETROVIR (zidovudine) to adult patients with early manifestation of ARC, including those presenting with only HIV-associated lymphadenopathy and a CD4 cell count < 500 cells/mm³.
2. To assess the efficacy of RETROVIR therapy in the treatment of HIV disease in these patients. Therapeutic efficacy will be determined by monitoring the following variables.
 - a. Changes in the incidence of progression of HIV disease to more advanced disease stages.
 - b. Changes in clinical manifestation of HIV disease as reflected in objective signs such as weight change, lymphadenopathy, Karnofsky score and performance on tests of neurologic function.
 - c. Prevention of the progressive deterioration of the immune response associated with HIV disease as reflected in changes in CD4 cell number and skin test reactivity.
 - d. Changes in levels of HIV viremia/antigenemia in virus-positive patients.

Technical Approach: The ability of RETROVIR to halt or delay early HIV disease progression is the critical clinical objective in the demonstration of therapeutic efficacy. clinical disease will be evaluated as described by the Centers for Disease Control classification system and the Walter Reed Staging System.

For the purpose of this study, the incidence of disease progression will be measured as follows:

1. By the development of severe ARC, characterized by a CD4 cell count < 200 persisting for a period of at least 3 months and the new development of at least 2 of the symptoms and/or infections listed in appendix VIII. *[Protocol 27,433-15/Project 53 Burroughs Wellcome Co.]
2. By the development of AIDS characterized by the diagnosis of any of the AIDS-defining diseases or disease-related conditions listed in Appendix III.
3. By an increase in Walter Reed classification of one or more stages.

Independent interim and final analyses of disease progression will be done using both systems.

Progress: MAJ Sun assumed PI responsibilities on 1 September due to MAJ Aronson's PCS. Ten patients have been enrolled; 5 were withdrawn. Two were dropped from the protocol secondary to progression (20% weight loss, dementia in one) despite low dose zidovudine so they could use higher dose. Three were withdrawn due to move from the area and not wanting to commute monthly to study site. FDA approved zidovudine Aug 90. No adverse effects have been recorded since Oct 90; all patients manifest macrocytosis.

As this protocol is part of a much larger multicenter study, local analysis of the limited number of patients is not particularly informative. However, all patients enrolled have manifested progression toward immunodeficient state over the past 2-3 years they have been on the protocol.

COL Harrison anticipates an addendum to protocol to extend it beyond 2 years to address the issue of zidovudine resistance.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/40

STATUS: Ongoing

TITLE: The Effect of Megestrol Acetate on the Cachexia of Human Immunodeficiency Virus Infection: A Randomized, Placebo-Controlled, Double-Blinded Study (Monitor: Dr. Lundy)

START DATE: Aug 89

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Wellington Sun

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Ms. Lynn B. McNicol, RN; PA Gregory Martin; 1LT Christine Norris, RD; Ms. Renata Riley, PA-C

KEY WORDS: Megesterol, HIV Wasting Syndrome

Study Objective: Assess the efficacy of megestrol acetate in the treatment of the anorexia and weight loss associated with HIV infection. Conduct a longitudinal analysis of nutritional, biochemical, anthropomorphic and psychosocial parameters in HIV patients receiving megestrol acetate.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Three patients were enrolled and completed the protocol: 1 gained 29# in 3 months; 1 lost 3# in 6 months; and 1 lost 5# in 6 months. One patient developed bilateral posterior subcapsular cataracts - irreversible after termination of Megace. MAJ Sun assumed PI responsibility on 1 Sep due to MAJ Aronson's PCS.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/51

STATUS: Ongoing

TITLE: A Treatment IND Protocol for the Use of Recombinant Human Granulocyte-Macrophage Colony Stimulating Factor (rGM-CSF) in Compassionate Circumstances (Monitor: COL Cannady)

START DATE: Jul 90

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Wellington Sun

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Ruben D. Sierra, MC; MAJ David C. Slagle, MC; MAJ Rieke Weickum, RPH; Ms. Lynn B. McNicol, RN

KEY WORDS: rGM-CSF

Study Objective: To offer Human rGM-CSF to patients with life threatening neutropenia (generally ANC < 500) due to an underlying disease or a therapeutic maneuver, and to assess the safety and tolerance of rGM-CSF in HIV and oncology/hematology patients.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: MAJ Sun assumed PI responsibility 1 Sep due to MAJ Aronson's PCS. A single HIV patient with severe neutropenia was entered for two courses over the past year. During the 2d course, the patient expired on the 3d day of therapy due to splenic rupture as a complication of disseminated pneumocystosis. Side effects were truncal and facial flushing during one infusion treatment with antihistamines and flu-like symptoms during the entire course. During the 1st course, the patient also experienced generalized erythema (mild) and low grade fever. On both occasions, in less than 1 week, he had an excellent return of neutrophils. Patient received 1st course in Oct 90 and did not need a 2d course until Feb 91.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/05

STATUS: Ongoing

TITLE: Active Immunization of Early HIV Infected Patients with Recombinant gp 160 HIV protein Phase II Study of Toxicity Immunotherapy, In vivo Immunoregulation and Clinical Efficacy (Monitor: COL Cannady)

START DATE: Nov 90

ESTIMATED COMPLETION DATE: Nov 96

PRINCIPAL INVESTIGATOR: MAJ Wellington Sun

DEPARTMENT: Med

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Charles E. Davis (WRAIR), MAJ John W. Kelly (DAHC); PA Gregory Martin

KEY WORDS: Recombinant gp 160 HIV Protein

Study Objective: To conduct a Phase II trial of the recombinant HIV envelope glycoprotein gp160 candidate vaccine, in patients with early HIV infection (Walter Reed Stage I-II). Specific objectives include:

- 1) To continue to evaluate the immunogenicity and toxicity of this product;
- 2) To determine the parameters predictive of immunoresponsiveness; and
- 3) To determine the clinical efficacy of immunization with gp160 in the treatment of early HIV infection.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Addendum: Modifies eligibility criteria. Approved by Tri-Service HUC (26 Feb 91), WBAMC HUC/IRB (23 Apr 91) and WRAMC HUC.

Amendment: Deleted recipe skin testing on Day 180 (typographical error). WBAMC IRB notified 16 Jul 91.

Amendment: Day 210 tetanus immunization shifted to Day 240 and Day 210 visit deleted. WBAMC IRB notified 17 Aug 91.

Progress: MAJ Sun assumed PI responsibility 1 Sep due to MAJ Aronson's PCS. Eight patients were enrolled. One patient withdrew after completing entry evaluation *before* receiving any vaccine because of a compassionate reassignment to Indianapolis, IN. He elected to wait for another (non-placebo controlled) immunotherapy study rather than commute to WRAMC. Seven patients remain in the protocol. All were rabies vaccine responders. Four are at day 180; one is at day 150; two are at day 120 of the protocol. One patient had significant fall (persistent) in CD₄ count to 328-340 range; all other remain >400 CD₄.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/53

STATUS: Completed

TITLE: Relationship of Childbirth Preparation Classes on Anxiety Levels of Primiparas: A Pilot Study

START DATE: Sep 90

ESTIMATED COMPLETION DATE: Dec 90

PRINCIPAL INVESTIGATOR: LTC Lorna Chatmon

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Karen R. Kurth, AN

KEY WORDS: Anxiety, Pregnancy

Study Objective: To determine the relationship between childbirth preparation classes and anxiety levels in primiparous women.

Technical Approach: The study design is non-experimental. Subjects will be placed in one of two groups. The first group will be those first time mothers who have attended formal, structured prenatal classes and the second group will be mothers who have not attended these classes. Because it could be ethically questionable to determine who can and cannot attend prenatal classes, the study is non-experimental, lacks randomization and uses a non-probability sample.

A biographical data-sheet will be completed prior to the administration of the State-Trait Anxiety Inventory. The questionnaires are self-administered and require minimal explanation. The biographical data sheet consists of general information. The STAI consists of 20 questions referring to state anxiety and 20 questions on trait anxiety. The questionnaires take approximately 20-30 minutes to complete. Data analysis will be done using nonparametric statistics to test significance at $p < .05$.

Progress: Pregnancy and childbirth is a situational crisis in the expectant mother's life when anxiety levels are expected to increase. In the past, anxiety in pregnancy has been demonstrated to have negative effects on the pregnancy. Childbirth preparation classes have become an accepted addition to patient education and are often thought to reduce anxiety. This pilot study consisted of 30 primiparous women with the control group being those who had no prenatal classes and the experimental group being those who attended classes. The study administered Spielberger's (1983) State-Trait Anxiety Inventory and a biographical data sheet. Frequency distribution and T-test were used to analyze the data.

Conclusion: There were no significant differences in trait anxiety scores between the two groups nor was there a significant difference in the mean state anxiety scores between the groups. When trait anxiety scores were compared to state anxiety scores individually, it was noted that the control group showed an increase in the state anxiety score of 12.5 points and the experimental group increased by only 4.9 points. This adds further support that prenatal education can be an important factor in reducing anxiety in primiparas.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/51

STATUS: Completed

TITLE: Death Education and Comfort Level of Perinatal Nurses

START DATE: Aug 91

ESTIMATED COMPLETION DATE: Aug 91

PRINCIPAL INVESTIGATOR: LTC Lorna Chatmon

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Susan Moreland, AN

KEY WORDS: Perinatal nurses

Study Objective: To determine if death education is a factor in improving the comfort level of perinatal nurses working with bereaved/dying patients, thereby improving the quality of patient care.

Technical Approach: This is an ex-posto facto survey. At change of shift, professional Registered Nurses working in the perinatal areas of L&D, 4P, 4G, Newborn Nursery and NICU will be given an explanation of the study prior to being invited to complete a questionnaire designed to measure comfort level in providing various types of care and interaction with bereaved or dying patients. Subjects will be given the option of completing the survey at that time or returning it within 24 hours. The study will continue until 20 subjects have been recruited.

Progress: Study was completed. The majority of the subjects were female ranging in age from 25-58 y/o. Nurses with death education did not differ significantly in comfort levels with dying and bereaved patients from nurses who had not received death education. However, generalization to a larger population regarding the effects of education on nurses' comfort levels should be tentative in view of the study limitations. The sample was one of convenience and the size was limited. The study should be replicated with a randomized and larger sample to strengthen the reliability and validity of these results.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/08

STATUS: Ongoing

TITLE: Relationships Among Selected Pre and Post-natal Factors and Perception of Birth

START DATE: Jun 90

ESTIMATED COMPLETION DATE: Oct 92

PRINCIPAL INVESTIGATOR: 1LT Clarke

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Deborah Oakley, Ph.D.

KEY WORDS: Pregnancy, Stress

Study Objective: To examine the birth experiences of civilian women who are married to active duty soldiers. The immediate and short range study aims will be to:

1. Identify perinatal factors which significantly influence and predict women's perceptions of their birthing experiences.
2. Explore relationships between the selected prenatal factors.
3. Communicate results to the military nursing community, military health care providers, and military leaders.

Technical Approach: A non-probability sample of 250 expectant mothers, planning to deliver and receive 6 week postpartum care at WBAMC will be obtained. Subjects will meet the following selection criteria: civilian, married to an active duty Army soldier, able to read and understand English, 32-38 weeks pregnant, experiencing an uncomplicated pregnancy, and anticipating her first delivery.

All prenatal clinic charts at WBAMC will be screened to determine subject eligibility. Data will be obtained prenatally and postnatally using mailed questionnaires and chart audits. An introductory mailing containing a cover letter, a stamped postcard, a stamped envelope, two copies of the informed consent, and questionnaire #1 will be sent to all eligible women. Questionnaire #2 will be sent to each subject approximately six weeks after her delivery as determined by either a returned postcard or a documented delivery. Hospital records of participating mothers and their infants will be reviewed in order to determine the presence of selected complications. Mothers may withdraw from the study at any time by indicating their desire to do so on the postcard provided and returning the postcard to the researcher. No additional data will be requested from subjects who choose to withdraw.

Progress: Approximately 24 subjects are enrolled and 10 have completed the entire study. Number of potential subjects decreased secondary to Desert Storm (decreased number of pregnancies). Analysis has not yet begun. 1LT Clarke assumed PI responsibilities due to MAJ Mauro's PCS.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/31

STATUS: Completed

TITLE: Patient Perceptions on Pain Intensity with Two Pain Control Modalities

START DATE: Jun 91

ESTIMATED COMPLETION DATE: Aug 91

PRINCIPAL INVESTIGATOR: CPT Gloria R. Long

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Pamela K. Burns

KEY WORDS: Pain perception

Study Objective: To determine whether differences exist in (1) perception of pain intensity between patients who receive opiate analgesics by PCA and those who receive opiate analgesics by IM injections and (2) expected pain intensity prior to surgery is different from actual experience for the PCA and IM groups; and if pain intensity scores (VAS) decrease as the number of analgesic doses increase for the PCA and IM groups.

Technical Approach: The is a descriptive-correlational design that will use the VAS scale and a questionnaire. The VAS scale and questionnaire are designed to determine the patient's level of pain and satisfaction with the postoperative pain experience. Twenty patients admitted for Anterior Cruciate Ligament (ACL) repairs to the knee will be selected over a 2-month period. Patients undergoing ACL repairs were chosen because of their homogeneity in health status, fewer postoperative complications and similar operative stress. Time and series measurements will be taken at 2-hour intervals of each participant's level of pain intensity with the VAS scale. Post-surgical questionnaire will examine the postoperative experience.

Progress: During the two month investigation, 6 subjects met the study criteria. Comparison of patients receiving IM injections versus those using PCA could not be carried out because all subjects in the sample received IM pain injections. The small sample size was a result of the limited age requirements and surgical procedure. PCA is not used for most patients after Anterior Cruciate Ligament (ACL) repairs. Variations in orthopedic surgical procedures and wider age range may have yielded a larger sample and differences in pain treatment modalities (PCA/IM). Resubmission of this study with changes in methodology is planned at a later date.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/43

STATUS: Ongoing

TITLE: Job Satisfaction in Clinical Head Nurses

START DATE: Jul 90

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: LTC Kathy Mauro

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Jerilyn A. Wadford, AN

KEY WORDS: Headnurse, Nurse, Job satisfaction

Study Objective: To describe the relationship between selected factors and overall job satisfaction in the Army Nurse Corps Clinical Head Nurse.

Technical Approach: A convenience sample of Army Head Nurses at William Beaumont Army Medical Center will be surveyed. The survey will be distributed to all ANC Head Nurses within the facility. An envelope will be provided and participants will be encouraged to complete the survey within 2 days. One week after initial distribution of the survey, each participant will receive a reminder encouraging them to return the survey if they have not already done so or thanking them if they have. Frequency distributions will be computed for all variables. Scores will be summed and divided by the number of items to attain a mean for each subscale. An overall means for the global scale will be attained as a general measure of nursing satisfaction. The data will be further analyzed using the demographics to assess differences in years of active federal service, specialty, sex, months as a head nurse, marital status, dependents, and work hours. Because of the use of a small sample, results may not be generalized to the Army Nurse Corps. The instrument to be utilized is recently developed. Personal variables cannot be controlled or documented because of subjectiveness of the survey.

Progress: Study complete with 24 subjects entered. Analysis in progress. Analysis being conducted by MAJ Wadford, ANC, Ft. Jackson, SC.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/03

STATUS: Completed

TITLE: The Examination of Feelings of Mothers of Premature Infants

START DATE: Sep 90

ESTIMATED COMPLETION DATE: Sep 91

PRINCIPAL INVESTIGATOR: MAJ Carol Neff

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Patricia A. Wilhelm

KEY WORDS: Mothers of premature infants

Study Objective: To identify the effects of a nursing intervention, contact with a neonatal nurse in the labor room, on the level of maternal anxiety associated with the birth of a premature infant. The following null hypothesis will be tested, H_0 : There will be no difference in anxiety levels of mothers of premature infants who have contact with a neonatal nurse during the labor period and mothers who do not have contact with a neonatal nurse.

Technical Approach: This quasi-experimental study utilizes a nonequivalent control group post-test only design with a time series approach. Subjects will be assigned to either a control or treatment group. The control group will be those mothers who deliver prematurely within one week from admission to the Labor and Delivery unit and who have no contact with a neonatal nurse while in labor. The treatment group will consist of those mothers who are in premature labor and who have contact with a neonatal nurse while in the early stages of labor and who also deliver within one week of admission to Labor and Delivery.

Progress: Study was completed and data analyzed.

Conclusion: Anxiety of mothers giving birth to premature infants has been well documented, but there has been little research regarding how to minimize this anxiety. This study was designed to evaluate whether a visit to the mother in preterm labor from an NICU nurse would have an effect on the mothers' anxiety level. Ten patients entered the study, five in the control group and five in the treatment group. Anxiety of these patients in the Recovery Room following delivery and again following the first visit to the baby in the NICU was evaluated using the STAI-S Anxiety Inventory using a four point Likert scale. The infants' neonatal risk was determined using Blumberg's Neonatal Risk Categorization Schema. The t-test was used to evaluate differences in anxiety levels between groups and revealed significant differences in anxiety both in the Recovery Room ($t = 3.15$, $df = 4$, $p = .04$) and following the first visit to the NICU ($t = 3.02$, $df = 8$, $p = .02$). There was no relationship between the infant's risk and the mother's anxiety level as evaluated by Kendall's tau. Based on these findings, a visit to a mother in premature labor by an NICU nurse can significantly reduce the anxiety of the mother, however, replication of this study with a larger sample is recommended.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/09

STATUS: Ongoing

TITLE: Assessment of Recalled Medical Reservists' Needs

START DATE: Dec 90

ESTIMATED COMPLETION DATE: Jan 92

PRINCIPAL INVESTIGATOR: MAJ Christine M. Piper

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Recalled medical reservists

Study Objective: To determine the degree of adjustment difficulty that reservists are experiencing and to assess the needs for additional support measures and programs.

Technical Approach: This study will utilize an anonymous voluntary questionnaire. This is a pilot study to survey medical and medical support reservists who were called to active duty to support Operation Desert Shield while assigned or attached to WBAMC.

Progress: Original PI conducted survey in January 1991 and was released from active duty in late January. MAJ Piper assumed PI responsibility, retrieved the data and will tabulate, analyze and report results.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/21

STATUS: Completed

TITLE: Satisfaction with Patient Controlled Analgesia

START DATE: Apr 91

ESTIMATED COMPLETION DATE: Jul 91

PRINCIPAL INVESTIGATOR: MAJ Susan D. Plumley AN

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Pamela K. Burns, AN

KEY WORDS: Analgesia

Study Objective: To determine patient satisfaction with degree of postoperative pain control using the patient controlled analgesia (PCA) infuser and to determine health care providers' use and knowledge of patient satisfaction with use of the PCA infuser.

Technical Approach: This study will focus on the current use of PCA as seen by the patient, nursing staff, and physician staff. Questionnaires will be given to all three groups. Subjects will be selected from the WBAMC narcotic registers. The first 40 patients from each of the four participating wards who have undergone a surgical procedure and received IV morphine or demerol through the PCA infuser over the 12-twelve month study period. The subjects will receive a letter, questionnaire, and consent form in the mail.

Upon receipt of the response and consent form, the investigator will extract pertinent data from the subject's inpatient record and the data will be statistically analyzed to determine if there is a relationship between patient satisfaction and the following factors:

- 1) prescribed PCA dose
- 2) prescribed lock out interval
- 3) nursing knowledge of PCA concept
- 4) nursing satisfaction with PCA
- 5) physician knowledge of PCA concept
- 6) physician satisfaction with PCA.

Amendment (Apr 91) included several changes recommended by a statistical consultant to enhance data analysis.

Progress: Project was completed and data analyzed. 160 surveys were mailed; 55 were returned. Overall, patients, physicians, and nurses are satisfied that PCA does control postoperative pain. However, the results indicate that physicians and nurses need to increase their understanding of the PCA concept. Literature reports indicated this is essential for success of PCA therapy. Current literature reports that PCA decreases postoperative complications, reduces hospital stay, and allows the patients to be more active during the day and obtain more rest at night. This study indicates that physicians and nurses do not agree with current literature reports. In addition, the average lock out interval (27.36 minutes) is well above that recommended by literature reports (6-10 minutes). Lastly, the literature emphasizes the importance of preoperative instruction regarding PCA use. This has not been done consistently on the four wards surveyed. Instructions have been given in the postoperative time period. When WBAMC introduced the PCA infuser in 1988, a class was given regarding the use of PCA and the PCA concept. This class was given on the test units where the PCA was to be used. It is recommended that a similar inservice education program be established that will update all nursing staff members on the current concepts of PCA. In addition, the physicians may benefit by adding use of PCA to their resident training curriculum.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/62

STATUS: Ongoing

TITLE: The Effects of Psychodrama, Large Groups and Small Groups, on Head Nurses' Burnout, Tedium

START DATE: Jun 89

ESTIMATED COMPLETION DATE: Dec 92

PRINCIPAL INVESTIGATOR: CPT B.J. Thomas

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Conrad Silvani, AN; CPT Danny Davison, AN; Mariva Barajas, DAC

KEY WORDS: Burnout, Anxiety, Work satisfaction

Study Objective: To empirically validate the use of the psychiatric techniques of using psychodrama, small group, and large group interventions by measuring the changes in burnout, anxiety, and work satisfaction.

Technical Approach: The subjects for this study will be the convenience sample of all the head nurses that attend the work shop "Stress and Burnout for Head Nurses".

Three instruments will be used in this study: The Tedium Measure, Spielberger's State-Trait Anxiety Self Evaluation Questionnaire, and Stamps-Piedmonte Index of Work Satisfaction.

Data will be collected using all three instruments at the beginning of the work shop after a brief welcome, introduction, and signing of the consent form. Demographic data will also be collected at this time. Only the Tedium Measure and STAI will be self-scored at this time. The results of these scores will be discussed in a large group atmosphere for the rest of the first hour.

The second hour will consist of psychodrama vignettes that all of the participants will have the opportunity to participate in using scripts that have been developed to portray typical difficulties on the nursing units. The scripts have been designed to demonstrate different leadership styles and attitudes that may be encountered on nursing units.

The third hour of the work shop will be small groups that will focus on the feelings and attitudes that the participants had when they were placed in the roles of the vignettes in positions other than the head nurse such as ward clerk, LPN, staff nurse, patient, etc.

The fourth hour will be a large group problem-solving discussion on how to improve attitudes, and decrease burnout and stressors by the inclusion of positive attitudes and conditions in the work place. All three of the instruments will then be re-administered at the end of the fourth hour.

Two weeks after the work shop each of the head nurses will again be administered each of the three instruments by the primary investigator.

The control group, which will consist of the head nurses that do not participate in the workshop, will be contacted on an individual basis and be administered the three instruments after signing a consent form and filling in the demographic data. The second administration of the instruments will take place approximately four hours after the first administration. The third administration of the instruments will take place approximately two weeks after the first two. No intervention will take place between the administration of the instruments.

All data sheets will be coded to protect the privacy of the participant. Only the primary investigator will have a master list of participant names and codes that will be secured at all times.

Progress: Data collection is complete. Analysis of data was in progress but interrupted by PCS move of PI. Data analysis will resume upon completion of PCS move and acquisition of suitable statistical support.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 86/24

STATUS: Ongoing

TITLE: The Effect of Relaxation Therapy on Patients with Asthma

START DATE: Jan 87

ESTIMATED COMPLETION DATE: Apr 92

PRINCIPAL INVESTIGATOR: Helen Villegas RN

DEPARTMENT: Nsg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Raghava Charya, MC

KEY WORDS: Asthma relaxation therapy

Study Objective: To measure the effects of relaxation therapy on asthma symptoms, frequency of prn medications, and emergency medical care.

Technical Approach: Fifty intrinsic asthma patients, 20-40 years of age, followed daily in the Allergy clinic, will be involved in participating in this pilot study for 6 weeks. History and biographical data will confirm the diagnosis of intrinsic asthma. Pulmonary function tests (PFT) will be measured on the first visit. PFT will also be recorded on the second and last visit. Patients will keep an asthma diary which will document daily peak expiratory flow rate, asthma symptoms, assessment of mood and use of prn medications and medical care. After 3 weeks, subjects will return to the Allergy Clinic with their completed diaries. Their PFT will be recorded. They will be instructed in the use of a relaxation tape to use each morning upon awakening and each night after retiring. This relaxation tape will include facial muscle exercises and positive thoughts and imaging. Medical news in the Journal of the Medical Association reported in 1983 that the imagination can be used to relieve asthma symptoms while Connors has concluded that tension changes in the facial musculature reliably influences the PEF. The patient will be given a new asthma diary to record the next 3 weeks. The hypothesis is that the relaxation therapy component of the patient's multifactorial therapy will improve asthma symptoms and decrease medication intake and the need for emergency medical care.

Progress: Fifteen patients are enrolled. Data from subjects receiving relaxation therapy has been collected. Control subjects were to be enrolled in Jan 91, however, enrollment was postponed due to unknown impact Desert Storm might have had on the Allergy/Immunology Service. The controls will be enrolled in the beginning of 1992 so that the data will be from the same period.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/24

STATUS: Ongoing

TITLE: Vaginal Hysterectomy; Morbidity with and without Injection of Epinephrine in the Vaginal Cuff

START DATE: May 91

ESTIMATED COMPLETION DATE: Apr 93

PRINCIPAL INVESTIGATOR: MAJ Philip C. Brittain

DEPARTMENT: OBGYN

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Andrew P. Soisson, LTC Carla Hawley-Bowland, LTC Harry C. Crawford

KEY WORDS: Epinephrine, vaginal cuff

Study Objective: To determine if vasoconstrictor use in vaginal hysterectomy increases the incidence of cuff infections and to determine if vasoconstrictor use significantly reduces blood loss during vaginal hysterectomy.

Technical Approach: Patients scheduled for elective vaginal hysterectomy will be prepared for surgery in the usual fashion. The cervicovaginal junction will be injected circumferentially in each patient with 10cc's of one of the solutions described below. All patients will be given similar antibiotic prophylaxis. Estimates of blood loss will be made in conjunction with operating room staff and anesthesia. Postoperative hematocrits will be drawn at similar intervals. Intravenous fluid replacements will be at a 3:1 ratio to estimated blood loss. Specific analysis of what constitutes a postoperative wound infection will be standardized; localized abscess, erythema, marked tenderness, temperature elevation, rising white blood cell count/increasing percentage of immature forms on peripheral smear, tissue necrosis, frank pus, temperature >38 c, negative chest x-ray, and negative cultures of blood and urine. Cuff closures will be standardized among surgeons in the study.

In a double blinded randomized fashion, the pharmacy at William Beaumont Army Medical Center will prepare and code the solution to be injected. The study group will be injected with a dilute solution of epinephrine (1:200,000) in sterile saline, and a control group with sterile saline. Only at the conclusion of the study will the code be broken and data analyzed.

Progress: 12 women have been enrolled. No adverse reactions have been noted thus far.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/47

STATUS: Ongoing

TITLE: The Clinical Management of Patients with Mild Dysplasia of the Uterine Cervix

START DATE: May 91

ESTIMATED COMPLETION DATE: Apr 93

PRINCIPAL INVESTIGATOR: MAJ Philip C. Brittain

DEPARTMENT: OBGYN

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Andrew P. Soisson, LTC Carla Hawley-Bowland, LTC Harry C. Crawford

KEY WORDS: Dysplasia (mild)

Study Objective: To determine the incidence of HPV infection in young women with histologically proven mild dysplasia (CIN I) of the uterine cervix.

Technical Approach: Patients with dysplastic cervical cells detected by cytology will undergo standard colposcopic examination, colposcopically-directed biopsies of suspicious cervical lesions found during colposcopy, and endocervical curettage. Patients with the following clinical and pathologic characteristics will be considered for study entry: (a) histologically proven mild dysplasia (CIN I) of the ectocervix; (b) adequate colposcopic examination; (c) absence of dysplastic epithelium in the endocervical canal as proven by endocervical curettage. These patients will be thoroughly counseled about study entry. Samples from patients who elect to participate will undergo in-situ DNA hybridization to detect specific subtypes of HPV within cervical cells using the Vira-Type kit. Patients with even last digit SSN will receive standard therapy using cryotherapy or laser vaporization of the transformation zone of the cervix (Group A). Patients with odd last digit SSN will be assigned to the observation group (Group B). All study participants will be monitored every 3 months in the Gynecology Clinic using cervical cytology (PAP Smear), colposcopic examination, and colposcopically directed biopsies of suspicious lesions. All women will be followed for a minimum of 2 years. The sexual partners of study group patients will be referred to the Male Dysplasia Clinic in the OB-GYN Clinic for Vira Type, colposcopy and colposcopically directed biopsies.

Progress: Study recently initiated. Two patients have enrolled.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/27

STATUS: Ongoing

TITLE: A Prospective Evaluation of Closure of Subcutaneous Tissue During Closure of Abdominal Incisions

START DATE: Jun 91

ESTIMATED COMPLETION DATE: Jan 93

PRINCIPAL INVESTIGATOR: CPT Jason P. Fontenot

DEPARTMENT: OBGYN

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Cesar Rosa

KEY WORDS: Incision, seroma

Study Objective: To evaluate whether closure of subcutaneous layer at the time of laparotomy closure has any effect on the incidence of hematoma, wound infection, or scar puckering.

Technical Approach: This study will be a prospective, randomized blinded study. Patients will be divided into two groups: (1) subcutaneous tissue will be closed with suture or (2) subcutaneous tissue will not be closed. Only the surgical team will know whether the procedure was performed. Daily evaluation of patient recovery will be performed during hospitalization. The incidence of wound infection, hematoma or abscess formation will be determined at the 6-week postop evaluation. Scar/incision condition and scar development will also be documented at 6 weeks.

Progress: Enrollment of subjects and data collection began in late August.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/25

STATUS: Ongoing

TITLE: The Association Between Race and Risk of Preterm Labor Among Enlisted Women

START DATE: May 91

ESTIMATED COMPLETION DATE: Feb 92

PRINCIPAL INVESTIGATOR: MAJ Frederick Harlass

DEPARTMENT: OBGYN

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CDR Melissa M. Adams (CDC)

KEY WORDS: Preterm labor

Study Objective: We propose a retrospective cohort study of the association between maternal race (black or white) and preterm delivery among the relatively homogeneous population of enlisted Army women who delivered at the four Army medical centers with the greatest number of deliveries. This study presents a unique opportunity to assess the relationship between race and a preterm delivery in a healthy, relatively homogeneous population for whom no financial barriers to prenatal care exist and in which the providers of and content of prenatal care are consistent across racial groups.

Technical Approach: We propose a retrospective cohort study of the association between maternal race (black or white) and preterm delivery among the relatively homogeneous population of enlisted Army women who delivered at the four Army medical centers with the greatest number of deliveries. This epidemiologic study presents a unique opportunity to assess the relationship between race and preterm delivery in a healthy, relatively homogeneous population for whom no financial barriers to prenatal care exist and in which the providers of and content of prenatal care are consistent across racial groups.

We plan to abstract data at four medical centers: Beaumont, Madigan, Walter Reed, and Tripler. Permission to review charts at each of these centers has been granted by the Office of the Surgeon General of the Army. We will abstract data from mothers and infant's charts. The study will include enlisted black or white mothers who delivered a live born infant of any gestational age or a stillborn infant of 20 weeks' gestation or longer from July 1, 1987 through September 31, 1990. We anticipate that most of the mothers will be aged 20-29 years. The infants will be newborns.

Progress: 469 subjects entered. The preterm delivery rate of active duty enlisted is 14% White and 15.8% Black. The is against a background rate of ~5-10% across the board for all pregnancies. National averages for all pregnancies is ~5-7% Whites and 17% Blacks, both working and non-working.

IMPRESSION: Early delivery is increased in both groups and no difference is noted in either the white or black race. More data to follow at other institutions. WBAMC data collection segment is complete. MAMC, TAMC, and WRAMC continued to collect data.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 86/08

STATUS: Ongoing

TITLE: OBGYN Bowel Training Utilizing the Pig Model

START DATE: Jul 86

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Carla G. Hawley-Bowland

DEPARTMENT: OBGYN

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Surgical training in Residency - GI

Study Objective: This training is designed to teach physicians the basic knowledge and operative skills required to perform basic small and large bowel surgery.

Technical Approach: The laboratory exercise described will concentrate on developing the surgeons confidence in recognizing bowel injuries, resecting and anastomosing small bowel, and large bowel exteriorization. To accomplish these training objectives, one survival and one non-survival surgical training procedure will be conducted on each animal assigned to the protocol. The first surgery consists of small bowel resection and re-anastomosis. The surgical site is then closed and the animal awoken from anesthesia. The surgical procedure and post operative care will be conducted as stated below. After approximately three weeks, a second laparotomy will be conducted and the training will consist of resecting the colon and creating a colostomy. Afterward, the surgical site will be closed and euthanasia administer while the animal is still anesthetized.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Eight pigs were utilized for training. Strict adherence to protocol guidelines is maintained.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 86/33

STATUS: Ongoing

TITLE: OB/GYN Microsurgical Tubal Re-Anastomosis Training Utilizing A Rabbit Model

START DATE: Mar 86

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Carla G. Hawley-Bowland

DEPARTMENT: OBGYN

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Cesar Rosa, MC

KEY WORDS: Tubal Re-anastomosis

Study Objective: This training is designed to teach resident physicians the basic knowledge and operative skills required to perform microscopic tubal surgery.

Technical Approach: The laboratory exercise described will concentrate on developing the surgeon's confidence in utilizing the operating microscope and microsurgical instruments as well as planning and accomplishing the operative procedures. To accomplish these training objectives, one survival and one non-survival surgical training procedure will be conducted on each animal assigned to the protocol. The first surgery consists of unilateral uterine cornua resection and re-anastomosis. The surgical site is then closed and the animal awoken from anesthesia. The surgical procedure and post operative care will be conducted as stated below. After approximately three weeks, a second laparotomy will be conducted. The first microsurgical anastomosis site will be re-explored for patency and the training procedure will be repeated on the contralateral cornua. After completion of the procedure euthanasia will be administered as described below.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Two rabbits were utilized. Strict adherence to protocol guidelines is maintained.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 86/64

STATUS: Ongoing

TITLE: Genitourinary Tract Surgery Training Utilizing a Pig Model and Comparing Stenting Technique

START DATE: Aug 86

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Carla G. Hawley-Bowland

DEPARTMENT: OBGYN

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Surgical Training

Study Objective: This training is designed to teach resident physicians the basic knowledge and operative skills required to perform genitourinary surgery while simultaneously evaluating the need for ureteral stenting following the operative procedures.

Technical Approach: The laboratory exercise described will concentrate on developing the surgeons confidence in recognizing GU injuries, resecting and anastomosing ureters, and reimplanting ureters into the urinary bladder. To accomplish these training objectives, one survival and one non-survival surgical training procedure will be conducted on each animal assigned to the protocol. The first surgery will consists of unilateral ureter resection and re-anastomosis. Upon completion of this procedure, the laparotomy incision will be closed and the animal awoken from anesthesia. The surgical procedure and post operative care will be conducted as stated below. After approximately three weeks, a second laparotomy will be conducted and the training will consist of transecting the contralateral ureter at the point of entry into the urinary bladder and reimplanting the ureter through the bladder wall. Afterward, the laparotomy incision will be closed and euthanasia administer while the animal is still anesthetized.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Six pigs were utilized. Strict adherence to protocol guidelines is maintained.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/63

STATUS: Ongoing

TITLE: Certification Training: Advanced Laser Laparoscopic GYN Procedures in the Porcine Model

START DATE: Sep 91

ESTIMATED COMPLETION DATE: Dec 91

PRINCIPAL INVESTIGATOR: LTC Carla Hawley-Bowland

DEPARTMENT: OBGYN

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Laser

Study Objective: To provide training and certification of OB-GYN Surgery Staff in laser and non-laser laparoscopic and vaginal surgical procedures. This training will enable them to develop the proficiency required to perform these operative procedures in human patients.

Technical Approach: The ability to suture during laparoscopy greatly expands the indications for laparoscopic surgery and increases the confidence of the surgeon performing more difficult procedures. There will be two live animal surgical stations and one station where some procedures will be taught with inanimate tissue such as bovine tongue and uterus. After the skin is prepped, an insufflation needle will be inserted near the umbilicus and the abdomen will be filled and maintained with 15mm Hg pressure of CO₂. The insufflation needle will then be removed and replaced with a trocar/cannula for introduction of the video laparoscope which will enable monitoring of the procedure on a video screen. Two to three additional trocars/cannulas will be placed for introduction of laparoscopic graspers, scissors, laser fibers, etc. Training will involve extracorporeal and intracorporeal suturing techniques of various urogenital tissue through the laparoscopic cannulas. The argon-beam and ND:YAG laser will be used to train in techniques of tissue coagulation and excision. Abdominal lymph nodes will also be excised laparoscopically. Training will be conducted on endometrial ablation and tumor excision procedures with lasers and electrosurgery (roller-ball and large loop wire electrodes) via a hysteroscope. If difficulty is encountered with introduction of the scope through the vagina, the uterus will be exposed by laparotomy via a mid anterior suprapubic abdominal incision. Additional training for endometrial ablation and tumor removal will also be conducted with bovine uterus and bovine tongue, respectively.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Training will proceed according to the protocol and the training agreement between WBAMC and Sierra Medical Center.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/48

STATUS: Ongoing

TITLE: Is Measurement of Antibody Excess Cost-Effective After Administration of Rh-Immune Globulin?

START DATE: Sep 91

ESTIMATED COMPLETION DATE: Jun 94

PRINCIPAL INVESTIGATOR: CPT George M. Kingsley

DEPARTMENT: OBGYN

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Frederick Harlass, MC

KEY WORDS: Rh-Immune Globulin

Study Objective: To perform cost analysis of the post-administration immune globulin excess testing.

Technical Approach: Patients entering the OB system will have ABO/Rh?Prenatal Antibody screen upon entry and at 28 weeks gestation (current standard practice). At delivery, patients identified as Rhogam candidates will be assigned by the attending obstetrician as being Low Risk (no gross placental pathology; no manual placenta extraction; no evidence of placental accreta, increta or percreta, and no evidence of placental abruption or placental previa) or High Risk (one of the above placental factors being present) for fetal-maternal hemorrhage. Patients will continue to receive post-partum Rhogam. Immune globulin excess monitoring will continue. An analysis will be performed to evaluate the cost-effectiveness of the post-administration monitoring for the total population, and comparing the High and Low Risk groups. The following methods of post-administration monitoring will be compared: Leihauer-Betke, Fetal-dex, ELAT (enzyme linked antiglobulin test), flow cytometry, and Rosette test.

Progress: Study just begun. No data to report.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 88/13

STATUS: Completed

TITLE: Accuracy of Transvaginal Ultrasound in the Diagnosis of Ectopic Pregnancy

START DATE: Jan 88

ESTIMATED COMPLETION DATE: Jul 89

PRINCIPAL INVESTIGATOR: CPT Vincent Lyons

DEPARTMENT: OBGYN

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Andrew W. Robertson; MAJ George G. SanMiguel; CPT Philip; LTC Marcia Kossman; LTC James Brown

KEY WORDS: Ectopic pregnancy, transvaginal ultrasonography

Study Objective: To compare the predictive accuracy of transvaginal sonography to transabdominal sonography in the diagnostic evaluation of patients with suspected ectopic pregnancies.

Technical Approach: One hundred unselected stable patients undergoing diagnostic work-up for a suspected ectopic pregnancy will be recruited to voluntarily participate in the study. Once enlisted in the study, they will receive a transvaginal sonogram utilizing a technique described by Brown, et al. in the antepartum diagnostic center. All transvaginal sonography will be performed by the attending or resident staff using an ultramark four ultrasound machine. A 3.5 MHZ end fire sector transducer covered with an aquasonic gel filled glove will be used. The information obtained will be retained in the ADC and blinded to the physicians who will then perform the standard diagnostic work-up. Once the patient's care is completed, her hospital chart will be reviewed for the information listed on the attached data collection record.

A Fisher exact test with a P of .05 will be used to compare the accuracy of the T/V to the T/A technique for predicting the presence or absence of an ectopic pregnancy.

Progress: Study completed with 50 subjects entered. The work was presented as an abstract at the 1989 Armed Forces District Meeting of the Am Coll of OB-GYN, Washington, DC, Nov 89.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/56

STATUS: Completed

TITLE: Comparison of Glucola v. Karo Syrup in the Performance of the One-Hour Glucose Screening Test

START DATE: Oct 90

ESTIMATED COMPLETION DATE: Jan 91

PRINCIPAL INVESTIGATOR: CPT Thomas E. Page

DEPARTMENT: OBGYN

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Frederick Harlass, MC

KEY WORDS: Glucola, Karo syrup, Glucose screening test

Study Objective: Devise a less expensive and more palatable way of performing the one hour glucose tolerance test.

Technical Approach: Approximately 50-60 patients will be investigated in a prospective manner. The study patients will be entered into the investigation in a random manner (method to be determined). The patients will serve as their own control. The patients will initially be tested with either the standard solution or the Karo syrup. The patients will then be retested during the following week with the comparative solution. The investigation will not be blinded. Statistical analysis will be performed by Student's T-test and any other applicable method. Exclusion: Insulin dependent diabetes mellitus. Ages will range from 18 to 45. All subjects will undergo thorough physicals as part of their routine obstetrical care as well as routine baseline CBC, Pap smear, RPR, Type and Rh, Cervical cultures, and rubella titers.

Progress: Forty-one patients were enrolled in the study; 3 withdrew due to nausea and vomiting. All patients underwent both a 50gm Glucola load, then a 50gm Karo syrup load and glucose (serum) levels were drawn for both tests.

Conclusion: There was no difference between the two substances for detecting abnormal glucose tolerance. The study was completed and a paper accepted for presentation.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/58

STATUS: Ongoing

TITLE: Gonadal Function After Vasectomy

START DATE: Nov 89

ESTIMATED COMPLETION DATE: Dec 91

PRINCIPAL INVESTIGATOR: LTC Cesar Rosa

DEPARTMENT: OB/GYN

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Neal Dunn, MC

KEY WORDS: Vasectomy, gonadal function

Study Objective: To evaluate whether there is any clinical or subclinical evidence of testicular function after vasectomy.

Technical Approach: Approximately 30 active duty males (or others) between the ages 25-40, having vasectomies performed by the Urology Service will be considered suitable candidates. There will be no blinding or randomization necessary. All subjects will receive the same tests. Each patient will serve as his own control. The following tests will be performed:

***Prior to vasectomy -**

1. Blood for Testosterone, FSH, LH, PRL, Estradiol. Serum to be frozen for future reference.
2. GnRH test: After the above is collected at - 0 min; similar samples will be obtained at 15, 30, 45, 60, 90 and 120 min after injection of 100 mcg of LHRH (Factrel, Ayerst Labs, New York) at 0 minutes.
3. Serum for antisperm antibodies. To document the incidence of antisperm antibodies following vasectomy. There is evidence of an increased incidence of antisperm antibodies in the circulation after vasectomies.
4. A total of 110ml of blood will be obtained per session (at time of vasectomy, then 6 and 12 months afterwards).
5. Testicular ultrasound to objectively measure size of the testicles.
6. Physical examination (as usual prior to surgery) and testicular size determination with orchidometers (particular attention to testicular tenderness or granuloma formation).

***The same tests will be administered at 6 and 12 months after the vasectomy.**

Progress: First GnRH injection prior to vasectomy has been completed on 11 subjects. Serum samples are frozen pending draw of second GnRH test post vasectomy. All samples will then be sent in batch to reference lab for analysis.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/17

STATUS: Ongoing

TITLE: A Prospective Study of the Treatment of Functional Ovarian Cyst

START DATE: Jul 91

ESTIMATED COMPLETION DATE: Apr 92

PRINCIPAL INVESTIGATOR: CPT Kenneth K.C. Vu

DEPARTMENT: OBGYN

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Cesar Rosa, MAJ Frederick Harlass

KEY WORDS: Functional ovarian cyst

Study Objective: To determine the effectiveness of oral contraceptives in the involution of benign ovarian cysts in a prospective, randomized fashion, comparing it with a population given placebo.

Technical Approach: Patients presenting to the Gynecology Clinic, who on examination are identified as having a suspected functional ovarian cyst, will be invited to join the study. If the patient accedes, randomization into an oral contraceptive versus placebo group will be performed. Prior to the initiation of medication, an endovaginal ultrasound will be performed by the Department of OB-GYN. The result of the endovaginal ultrasound will not affect the treatment of the patient. As a second arm to the study we will derive information which will indicate how effective is the physician's bimanual examination as compared to the endovaginal ultrasound in the identification and follow-up of these functional ovarian cysts. The patient will be followed for 8 weeks or two cycles with an examination both by bimanual examination and endovaginal ultrasound at the end of 4 and 8 weeks of treatment or placebo.

Progress: Sixteen patients have been enrolled. Enrollment is lower than expected due to lack of patients who meet the study criteria. There have been no complications.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/30

STATUS: Ongoing

TITLE: Accupressure Bracelets: An Effective Treatment for First Trimester Nausea and Vomiting of Pregnancy

START DATE: Aug 91

ESTIMATED COMPLETION DATE: Aug 92

PRINCIPAL INVESTIGATOR: CPT Gary Wharton

DEPARTMENT: OB/GYN

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Dan L. Gehlbach, MAJ, MC

KEY WORDS: Accupressure bracelets, Nausea, Vomiting of pregnancy

Study Objective: To investigate whether the use of an acupressure bracelet can effectively treat nausea and vomiting associated with first trimester gestation.

Technical Approach: Pregnant women who complain of significant nausea and/or vomiting for at least one week's duration will be eligible for this study (dependent daughter's under the age of 18 will be excluded from the study as minors). Patients with other identifiable causes of nausea/vomiting, such as viral syndrome, molar pregnancy, thyroid disease, or preexisting gastrointestinal disease, will be excluded. Patients who are unmarried and less than 18 years of age will be excluded, as will those who require hospitalization on their initial presentation to the clinic. Entry to the study will be offered to all eligible patients at their New OB physical, and to patients presenting to the OB Walk-in Clinic who complain of morning sickness. 75 patients will be randomized by card flip into 3 study groups of 25 patients each. Group 1 will consist of dietary instruction alone; Group 2 will receive dietary instruction and the accupressure bracelet; and Group 3 will receive dietary instruction and the placebo bracelet. Specific oral and written instructions will be given by the authors on correct wear of the bracelets: the accupressure bracelet is to be worn snugly against the arm at 3 fingerbreadths above the wrist flexor crease with the bead against the flexor tendons; the placebo bracelet is to be worn at the level of the wrist flexor crease and loosely enough that a finger may be easily slid beneath the band.

On initial presentation and at each of two weekly visits the patient will be weighed on the same scale in the OB-GYN Clinic, and a questionnaire (Figure 1) administered by an independent observer. The authors will review treatment aspects and record routine obstetrical data at each visit. Patients will be given handouts with specific dietary/treatment instructions and will be asked to record prospectively the number of episodes of emesis. Each patient will be followed for 2 weeks.

Additional support will be required by the Brace Shop in preparation of the placebo bracelets.

Progress: Project is ongoing with 20 subjects enrolled at a rate of approximately 5-6 entrants per month. Three patients withdrew secondary to schedule conflicts. No complications have been encountered.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/28

STATUS: Ongoing

TITLE: Evaluation of Phenobarbital in the Prevention of Intraventricular Hemorrhage in the Very Low Birth Weight Infant (<1500gms or 32 Weeks)

START DATE: Oct 91

ESTIMATED COMPLETION DATE: May 92

PRINCIPAL INVESTIGATOR: CPT Gary C. Wharton

DEPARTMENT: OBGYN

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Frederick E. Harlass, MC

KEY WORDS: Intraventricular hemorrhage, phenobarbital

Study Objective: To retrospectively compare WBAMC records where the current standard of care includes phenobarbital administration to any mother suspected or imminently delivering an infant 15gms or less, to those of R. E. Thomason General Hospital (RETGH), where the current standard of care does not include this administration. Through this comparison, an attempt will be made to demonstrate that such administration is beneficial in reducing the incidence and severity of intraventricular hemorrhage in this population as previously suggested.

Technical Approach: This will be a retrospective case controlled analysis of maternal and infant records. WBAMC's experience will be controlled with the experience at RETGH.

Progress: Study was approved to begin upon approval of the RETGH IRB.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 87/83

STATUS: Terminated

TITLE: Analysis of Hospital Bacterial Pathogens - Chromosomal and/or DNA Fingerprinting

START DATE: Oct 87

ESTIMATED COMPLETION DATE: Jul 91

PRINCIPAL INVESTIGATOR: CPT Thomas Casey

DEPARTMENT: Path

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Michael Lieberman, MS; CPT David Smith, MS

KEY WORDS: DNA, Pathogens, Epidemiology, Nosocomial Infection

Study Objective: Identification of bacterial strains by subjecting plasmid DNA or chromosomal DNA to restriction endonuclease digestion and then agar gel electrophoresis.

Technical Approach: Plasmid DNA fingerprinting. Methods for plasmid DNA fingerprinting have been described in the literature. A typical method involves isolation of plasmid DNA by lysis and centrifugation. The plasmid DNA is digested with restriction endonuclease. The resultant DNA fragments are analyzed by agarose gel electrophoresis and the pattern obtained from different isolates and compared. Electrophoresis patterns obtained will be compared by visual inspection; thus, statistical analysis is not required.

Progress: This protocol was terminated due to PCS move of staff advisor and non-viability/contamination of 4-5 year old cultures.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 88/76

STATUS: Terminated

TITLE: In vitro Studies of Bactericidal Activity Associated with Specific Antibody to Pseudomonas aeruginosa Ribosomal Vaccine and Bactericidal Protein(s) Extracted from Live P. aeruginosa

START DATE: Nov 88

ESTIMATED COMPLETION DATE: Jul 91

PRINCIPAL INVESTIGATOR: LTC Michael M. Lieberman

DEPARTMENT: Path

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Pseudomonas aeruginosa, Bactericidal protein

Study Objective: (1) To determine the extent of bactericidal activity associated with specific antibodies directed against P. aeruginosa ribosomal vaccines. (2) To characterize the bactericidal "blocking" or inhibiting activities observed in specific antiserum to such vaccines. (3) To further characterize the nature and effects of bactericidal proteins extracted from live P. aeruginosa, and their interaction with bactericidal antibodies.

Technical Approach: In vitro bactericidal and opsonophagocytic assays. Murine antisera to ribosomal vaccines have been prepared previously and are available for use. The bactericidal and opsonophagocytic assays have been described in detail. Briefly, the assays involve mixing combinations of bacteria, antiserum (or IgG purified from antiserum by commercially available Protein A affinity chromatography or ion exchange chromatography methods), complement, and phagocytic cells (for opsonophagocytosis). (Phagocytes, i.e., polymorphonuclear leukocytes are prepared at the time of the experiment from a normal human volunteer.) After incubation of the mixtures, aliquots are spread on agar plates to determine the number of viable bacteria (colony forming units) remaining in the reaction mixtures. This number is compared with the initial inoculum in the mixture to determine the relative bactericidal or opsonic capability of the antiserum or IgG being tested.

"Blocking" activity is observed when the addition of more antiserum or purified IgG to a reaction mixture results in less (or no) bactericidal activity than is obtained without the additional antiserum or IgG. Thus, if experiments are performed in which bactericidal or opsonic activity is determined as a function of the concentration of antiserum or purified IgG, in some cases a "prozone" is obtained, i.e., maximal bactericidal activity is found at intermediate concentrations of antiserum or IgG, with significantly less activity at both higher and lower concentrations. Furthermore, it may be shown that IgG purified by one method from an antiserum which exhibits this "prozone" effect also demonstrates the same effect, whereas IgG purified by a different method from the same antiserum no longer exhibits a "prozone" at the same concentrations of IgG.

Interaction of protein extracts of P. aeruginosa with antiserum and purified IgG. Bactericidal and opsonic reaction mixtures will be set up including the proteinaceous, aqueous extracts in addition to antiserum or IgG. In these cases, the extract by itself has no bactericidal activity against the particular strain of P. aeruginosa used, and the antiserum or IgG by itself also demonstrates no such activity. However, when mixed together, bactericidal activity may appear.

Progress: No new data collected since last year. Project terminated due to PCS of principal investigator.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/45

STATUS: Ongoing

TITLE: Comparison of Two Techniques of Estrogen Receptor Assay in Breast Cancer

START DATE: Nov 89

ESTIMATED COMPLETION DATE: Jun 92

PRINCIPAL INVESTIGATOR: CPT Ann R. Price

DEPARTMENT: Path

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Tu Huu Nguyen, MC; CPT Gordon Bell, MC; LTC Steven Army, MC

KEY WORDS: Estrogen receptor assay, breast cancer

Study Objective: To confirm that the immunohistochemical assay is as reliable as the biochemical assay in determining estrogen receptor content in human breast cancer and to determine whether the immunohistochemical assay would be a more efficient method to perform at William Beaumont Army Medical Center than shipping specimens to another laboratory for biochemical assay.

Technical Approach: The study will consist of two phases which can be performed simultaneously.

Phase I: Phase I will be a retrospective evaluation of the estrogen receptor content of the paraffin embedded tissue blocks of the 50 most recently diagnosed breast cancers at WBAMC. The paraffin imbedded tissue will be pre-processed with the Trypsin and Dnase and the immunohistochemical assay will be performed by a single technician. The slides will then be scored in a qualitative and semiquantitative manner as outlined by Cudahy, et.al., and Pertshuk, et.al. Tumors found to contain more than 10% estimated positive cancer cells will be considered estrogen receptor positive. An ocular grid on the microscope will aid in accurately assessing tumor cellularity. The semiquantitative evaluation will be calculated by estimating the intensity of the nuclear staining as 1+, 2+, or 3+ of 200 cells and then multiplying 1, 2, or 3 by the percentage of cells estimated at each intensity. This figure will then be adjusted by multiplication with the previously estimated cellularity values less than 5 will be "zero-trace", 5-18 will be "low-intermediate", and greater than 18 will be "high". The biochemical assay results are expressed in femtomoles (FMOL) of receptor per microgram of DNA. Tumors with values less than 0.10 FMOL will be considered "negative", 0.10-0.30 FMOL will be "low-intermediate", and greater than 0.30 FMOL will be "positive". The results of the two techniques will be compared to determine concordance. All statistical analyses will be performed by means of the chi-squared test.

Phase II: Phase II will be a prospective, blinded evaluation of the estrogen receptor content of breast carcinomas by two methods - the immunohistochemical technique using the Abbot Kit (ERICA) and the biochemical assay done by PathLab. Each breast biopsy specimen is received in the fresh state in the Pathology Department at WBAMC. Standard operating procedure will be followed and a frozen section will be performed if the specimen is grossly suspect for cancer. Once a diagnosis of cancer is made histologically, additional frozen sections will be cut for immunohistochemical processing for evaluation of estrogen receptors. If the specimen contains sufficient tissue for biochemical assay (at least one cubic centimeter of tumor), a specimen will be sent to PathLab for evaluation as per usual procedure. The remaining specimen will be processed as usual into paraffin embedded blocks for histochemical viewing. Additional sections will again be made for immunohistochemical evaluation also. One histochemical technician will process the special staining as is standard operation in the WBAMC Pathology Department. The slides processed on frozen and paraffin embedded tissue will be read by all pathologists in the department, depending upon the rotational schedule assigned. The evaluators of the slides will be blinded to the results from the PathLab assay. The frozen and paraffin embedded immunohistochemical slides will be evaluated on different days, thus allowing different evaluators to be blinded to the previous result. The results will be reported as previously outlined

in phase I. results of the immunohistochemical assays on both fresh frozen and paraffin imbedded tissue will be compared to each other as well as to the results of the biochemical assay to determine concordance. The cost and time involved to obtain a report of the results will also be compared in order to determine the efficiency of the immunohistochemical assay. As stated previously, this study may eventually be expanded through screening of medical records to determine if the immunohistochemical assay is as effective in predicting the response to hormonal therapy as the biochemical assay since this is the ultimate goal of any estrogen receptor assay.

Progress: Progress has been slow due to initial problems in obtaining supplies. Then problems with technical assistance arose delaying the numbers of specimens processed to date. Forty-five cases have been entered to date which is lower than the number anticipated. The PI feels sufficient numbers can be obtained over the next year for completion of the study.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/04

STATUS: Ongoing

TITLE: Adolescent Females with Hirsutism and/or Menstrual Abnormalities Suggestive of Polycystic Ovarian Syndrome or Late Onset Congenital Adrenal Hyperplasia

START DATE: Oct 90

ESTIMATED COMPLETION DATE: Jul 92

PRINCIPAL INVESTIGATOR: CPT Suzanne E. Cuda

DEPARTMENT: Peds

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Rita L. Svec

KEY WORDS: Hirsutism, Menstrual abnormalities, Polycystic Ovarian Syndrome, Congenital adrenal hyperplasia

Study Objective: To prospectively follow patients with the complaints of hirsutism and/or menstrual abnormalities using standard of care. The data collected from these patients will be collated and compared to previous studies in an attempt to clarify prior research and work out a more streamlines approach.

Technical Approach: Females presenting to the Adolescent Clinic with complaints of hirsutism and/or oligomenorrhea and amenorrhea will be eligible for the study. Patient must be two years past menarche. Patients will sign an informed consent which will allow data collected during their care to be used in a study. Diagnostic work-up and treatment will be according to the accepted standard of care. We propose to combine several approaches to the work-up of these complaints in order to elucidate more information concerning the differences and similarities between patients falling into a particular diagnostic category.

Progress: Twenty-five patients have been enrolled to date. Enrollment, data collection and treatment per protocol are ongoing.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/35

STATUS: Ongoing

TITLE: A Double-Blind Randomized Trial of Low Dose Captopril in Adolescents with Insulin-Dependent Diabetes Mellitus

START DATE: Jul 91

ESTIMATED COMPLETION DATE: Jul 93

PRINCIPAL INVESTIGATOR: CPT Suzanne E. Cuda

DEPARTMENT: Peds

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Rita Svec

KEY WORDS: Captopril, Adolescent insulin-dependent DM

Study Objective: To examine adolescent diabetics with persistent microalbuminuria to determine if use of an ACE inhibitor can reduce microalbuminuria.

Technical Approach: On entry into the study, 3 specimens for microalbuminuria and a 24-hour urine specimen for protein and creatinine will be obtained. The mean of the 3 microalbuminuria samples will be used to determine persistent microalbuminuria. If abnormal, the subject will be eligible to participate in the study. Baseline HgA1C, CBC/diff, TFTs, renal functions, and ophthalmology exam will also be documented. Patients will be randomized using a random numbers table into treatment or placebo groups. This will be double-blinded. The treatment group will be started on Captopril at 0.1 mg/kg/dose twice daily. The placebo group will receive similar tablets twice daily. At the end of six months, the groups will cross over and complete the remaining six-month period. Subjects will be followed every 6-8 weeks with measurement of blood pressure, microalbuminuria, HgA1C, renal panel, and 24-hour urines. Compliance with the medication will be followed by counting pills. The treatment period will be 12 months for each subject. Following treatment period, subjects will return in 6-8 weeks for measurement of blood pressure, HgA1C, and microalbuminuria. Results will be analyzed using the paired Student t test.

Progress: No patients enrolled to date. PI still testing to establish eligibility for protocol entry.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/08

STATUS: Ongoing

TITLE: Seasonal Occurrence of Adolescent Health Risk Indicators

START DATE: Jan 91

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: COL John D. Foley

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Health risk indicators

Study Objective: To determine if certain indicators of health risk behaviors by adolescents show a seasonal pattern of occurrence.

Technical Approach: Data will be collected retrospectively from outpatient and inpatient clinical records of information previously recorded in the course of providing appropriate medical care for patients. No identification of individuals by name will be necessary. Data from the previous 2-3 years will be utilized as available. Major areas of focus will be sexuality, substance use, and psychologic problems.

Progress: Project was temporarily interrupted by departure of LTC Imai (PI). COL Foley will assume role of PI and continue the project.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/06

STATUS: Ongoing

TITLE: Perceived Susceptibility to Harm During Adolescence

START DATE: Oct 89

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: COL John D. Foley

DEPARTMENT: Peds

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Lawrence D. Cohn, Ph.D.

KEY WORDS: Risk taking behavior

Study Objective: The aim of the proposed research is to determine if teenagers hold exaggerated beliefs about their ability to avoid injury and illness. Such unrealistic optimism has been found to characterize the judgments of adults, and the proposed research seeks to determine its developmental course during early-, middle-, and late-adolescence. Although established procedures exist for assessing unrealistic optimism, these procedures have not been employed with adolescents. The proposed research will fill this gap. In so doing, the research will test the frequent assertion that teenagers overestimate their own invincibility.

A second objective of the research is to determine if unrealistic optimism contributes to the initiation of adolescent substance use, reckless driving, and other health threatening activities. The association between risk-taking and unrealistic optimism will be examined in adolescents in the general population, as well as adolescents who have been hospitalized due to injuries arising from their own risk behaviors. The goal of this comparison is to determine if teenagers who are unsuccessful at avoiding harm (i.e., hospitalized teens) display the greatest degree of optimistic bias.

A third objective of the research is to determine if unrealistic optimism diminishes when adolescents evaluate dangers for which they are at unique risk. In particular, the study seeks to determine if Hispanic, Black, and White youth show diminished optimism when evaluating the health threats associated with their respective ethnic background (e.g., increased threat of diabetes among Hispanics).

The final objective of the research is to determine if two developmental variables, age and ego development, influence the magnitude of unrealistic optimism displayed by adolescents.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Analysis of data is in progress on this collaborative project between WBAMC and UTEP. LTC Imai departed and COL Foley will assume PI role at WBAMC and continue the project.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 88/29

STATUS: Ongoing

TITLE: Ceftriaxone for Outpatient Management of Suspected Occult Bacteremia (Monitor: COL Popejoy)

START DATE: Apr 88

ESTIMATED COMPLETION DATE: Dec 92

PRINCIPAL INVESTIGATOR: CPT Anna I. Helser

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Suzanne Cuda, M.D., Robert Goldbach, M.C.

KEY WORDS: Ceftriaxone, occult bacteremia, pediatrics

Study Objective: To compare the effectiveness of ceftriaxone versus augmentin in the treatment of children with a possible blood infection.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Collection of data is progressing well with increased enrollment of study subjects (150).

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 88/61

STATUS: Ongoing

TITLE: Neonate Emergency Procedure Training in the Rabbit and Guinea Pig Model

START DATE: Jul 88

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Steven W. Jesse

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Emergency procedures, Pediatric training

Study Objective: To train physicians who have not been previously trained in emergency management of neonates, but who will be called upon to perform this function in the Neonatal Intensive Care Unit. The rabbit model will simulate the full term human neonate; the guinea pig model will simulate the preterm human neonate.

ADDENDUM #1: Additionally, the rabbit model will be utilized to demonstrate the procedure for instituting and maintaining an infant on an Infrasonic's Infant Star high frequency ventilator.

Technical Approach: This training is designed for junior house staff who are inexperienced in the management and emergency care of sick infants. Demonstration by a staff neonatologist of the various procedures to be learned will be performed before any hands-on attempts by the interns and residents. The housestaff will then rotate through practical skill stations to perform the assigned tasks. The skill stations and animal lab allow the student to observe and practice to proficiency those life-saving skills necessary in the management and stabilization of the neonatal patient. The animal lab will be held on two separate days with a staff neonatologist and staff veterinarian present on both days.

ADDENDUM: If HFV training is to be provided, then following the administration of anesthesia the staff veterinarian or neonatologist will place a carotid artery catheter as follows: A 3 cm ventral longitudinal skin incision will be made in the mid-cervical region. The 2 cm segment of carotid artery will be isolated by sharp and blunt surgical technique. A proximal and a distal 3-0 silk tie will be passed around the carotid artery. After the distal tie is ligated, a 20 ga catheter will be placed into the carotid artery and directed proximally. The proximal tie will then be secured and the catheter will be sutured to the skin. The skin incision will be closed and the patency of the catheter will be maintained with a heparin lock to enable periodic arterial blood collection for blood gas analysis.

High frequency ventilation: While anesthetized, an intubated rabbit will be placed on an Infrasonic's Infant Star HFV, initially on a conventional IMV mode. Monitoring will be done by chest auscultation and arterial blood gas analysis in the Biological Research facility. HFV will be instituted following the Infrasonic's lab outline. The animal will remain in this mode while the ventilation strategy is thoroughly explained and demonstrated to the participating personnel.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, analgesics, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Three animals have been utilized. Training procedures have strictly followed existing protocol and has been well received by trainees. Competency is judged by staff observation prior to interns beginning clinical rotations. Training is conducted on an annual basis for each intern class with provisions with provision of a mid-year remedial lab for those who lack required competence.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 88/65

STATUS: Ongoing

TITLE: Pediatric Intubation Training Utilizing the Feline Model

START DATE: Jul 88

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Steven W. Jesse

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Intubation, pediatric training

Study Objective: This training is designed to teach physicians and other health care professionals basic knowledge and endotracheal intubation skills required to resuscitate a neonate (newborn) or infant.

Technical Approach: The laboratory exercise described below will concentrate on developing the health professional's confidence in establishing an airway. Each new house officer will be required to intubate 2 cats employing a laryngoscope and endotracheal tube.

Animals will be anesthetized with ketamine HCL (22 mg/kg, given intramuscularly), with atropine (0.04 mg/kg, subcutaneously). Up to 2 additional half-doses (11 mg/kg) of ketamine may be given if needed. Pre-anesthesia with tranquilizer (Acepromazine, 0.2 mg/kg, subcutaneously) may be given to allow easier intubation for first-time trainees. Administration and monitoring of anesthesia will be directly supervised or performed by the attending veterinarian. The veterinarian will be present at all times to assist, modify, or terminate the procedure. Butorphanol tartrate (0.2 mg/kg SC every 8 hours) will be administered after the procedure to alleviate any possible pain.

At the discretion of the instructor, the stages and planes of anesthesia may be defined and assessed by the students. The animal will be placed in dorsal recumbency. Each trainee will visualize the larynx, noting the similarity of the feline larynx to that of the human infant; palpate the larynx externally; and perform visual intubation using the laryngoscope and endotracheal tube.

Two animals will be intubated by each first-time trainee in each laboratory session. Previously trained individuals will use one animal.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Two animals have been utilized. Semiannual use of felines to train pediatric housestaff in emergency life saving (and invasive) procedures has been expanded to include selected obstetrics housestaff and senior NICU nursing personnel. Felines are used solely for intubation training. Training procedures have strictly followed existing protocol and has been well received by trainees. Competency is judged by staff observation. Will continue with annual review for all selected incoming personnel.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/92

STATUS: Ongoing

TITLE: The Effect of Breastfeeding on the Enteral Absorption of Human IgG in the Neonatal Hartley Guinea Pig

START DATE: Oct 89

ESTIMATED COMPLETION DATE: Jun 92

PRINCIPAL INVESTIGATOR: MAJ Steven W. Jesse

DEPARTMENT: Peds

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Breastfeeding, Enteral Absorption of Human IgG, Human IgG

Study Objectives: To assess the influence of breastfeeding on the enteral absorption of immunoglobulin in the neonatal guinea pig. And to assess whether such enterally absorbed immunoglobulin retains function in the form of opsonic activity against Type III Group B Streptococcus.

Technical Approach: Multiparous, untimed-pregnant Hartley guinea pigs will be obtained from a commercial source. Dams will be allowed to deliver pups vaginally at term. Pups will be randomly assigned to receive all nutrition via either suckling, (Group A), or via a commercially available animal formula, (Group B). Appropriate nutritional additives (vitamin C, etc.) will be added to the formula by the veterinary staff. Pups in each group will be gavaged shortly after birth with a single dose, 3g/kg(3cc/100g) 10% Human IgG obtained through a commercial pharmaceutical company. This unit dose has been demonstrated in past investigations to result in consistent enteral absorption of enough Human IgG to be easily detected by current methods of analysis. Serum samples will be collected at 1, 2, 3, 7 and 14 days following the administration of the IgG. Sera will be separated and stored at -4 degrees C until analysis. Positive controls will consist of values from sera obtained from animals from prior investigations who were injected with Ig/kg 10% HIgG intraperitoneally. Negative controls will be derived from sera pooled from dams and stillbirths during this current investigation.

Lab analyses:

Serum total Human IgG: Competitive Inhibition

Enzyme Immunoassay (25)

IgG Opsonic Activity: Opsonophagocytic Assay (26)

Volume required:

30 uL sera (60 uL blood) per assay

2 assays/sample = 120 uL (0.12 ml)/sample

5 samples/animal over 14 days = 0.6ml total

Estimated blood volume of newborn guinea pig =

7cc. Blood requirements are thus minimal.

Addendum: 16 Mar 90 - Added Objective: to better define the timing of gut closure for the enteral absorption of human IgG in the neonatal guinea pig. Method: Newborn Hartley guinea pig pups will be randomized to receive human IgG orally at the following times: birth, 24 hours of age or at 48 hours of age. Pups will also be randomized to be either exclusively breast or formula fed (as per the current protocol).

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Approximately 52 guinea pigs have been utilized. Animal work has been completed. Extensive serum analysis is pending PI receiving protected research time from clinical duties to complete the protocol.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/91

STATUS: Ongoing

TITLE: Protocol for Determining the Prevalence of Drug Affected Babies in the Military Population

START DATE: Oct 89

ESTIMATED COMPLETION DATE: Oct 92

PRINCIPAL INVESTIGATOR: CPT Scott Knight

DEPARTMENT: Peds

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CPT Howard Oaks, MC; CPT Bill McGrail, MC; MAJ Frank Galin, AN; CPT Gordon Bell, MC

KEY WORDS: Newborn, Drug Affected

Study Objective: To determine the prevalence of the use of illicit drugs during pregnancy in a military population.

Technical Approach: This study is to include all pregnant women who present in labor at WBAMC over a 4 month period or 400 patients, and the infants they deliver.

There will be 400 subjects. Two study groups; mothers and infants. A urine drug screen for marijuana, PCP, cocaine and heroin will be done on all subjects. The drug screen is an enzyme immunoassay. This is a test that is not normally done on these type patients. Urine will be collected from all mothers upon admission to labor and delivery, and frozen. All newborn's first void will be collected with a urine bag and frozen. Biweekly both sets of specimens will be sent to toxicology and assigned study identification numbers. The assay will then be performed.

Data will be collected weekly from the toxicology section of the laboratory and analyzed to determine the prevalence of positive drug screens in the mothers and the infants.

Progress: Sixty samples have been collected. CPT Knight assumed PI responsibility from CPT Helser.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/40

STATUS: Complete

TITLE: Measles Immunity in New Housestaff

START DATE: Jun 91

ESTIMATED COMPLETION DATE: Nov 91

PRINCIPAL INVESTIGATOR: CPT Keith P. Ramsey

DEPARTMENT: Peds

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Schydlower

KEY WORDS: Measles, personnel health care

Study Objective: To determine the prevalence of immunity to measles in a group of health care workers, who are also young adults; to ensure immunity of new housestaff associate investigators; and to be cost-effective in immunizing new housestaff.

Technical Approach: A questionnaire will be administered to newly arriving interns at WBAMC to determine their past history with respect to measles infection. Immunization records will be reviewed to assess the number and timing of immunizations to measles. Sera will be drawn on each new intern for determination of individual immunity using ELISA.

Progress: 44 of 45 interns had blood drawn. PI has serology on Rubeola, Rubella varicella on 44 of 44 and anti-HBSAG on 41/44. PI notified C, Infect Dis of interns with low or negative hepatitis-B antibodies so they could be notified for boosters. PI to conduct more literature research and obtain remaining data needed for study completion.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/55

STATUS: Ongoing

TITLE: Parents Opinions about Disorders of Vigilance in their Children with Attention Deficit Disorder

START DATE: Aug 91

ESTIMATED COMPLETION DATE: Jan 92

PRINCIPAL INVESTIGATOR: MAJ Leslie A. Richardson

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Alva W. Atkinson

KEY WORDS: Vigilance, attention deficit

Study Objective: Through the use of a parent questionnaire, determine the incidence of symptoms of Primary Disorder of Vigilance (PDV) in a population previously diagnosed with Attention Deficit Disorder (ADD) or being evaluated for ADD. Furthermore, this project will seek to differentiate this symptom cluster (PDV) as either a unique diagnosis or a subtype of ADD.

Technical Approach: The Developmental Pediatric Clinic at WBAMC follows approximately 180 patients with the diagnosis of ADD. Patients who are taking medication for ADD are seen in clinic at least every three months and parents come in for a brief interview on progress and refill every month. During one of these routine follow-ups, the parent will be asked to complete a questionnaire which addresses the major criteria for PDV for both the child and his/her parents. These criteria are taken directly from the article "Primary disorder of vigilance: A novel restlessness, and sleepiness" by Weinberg describing this "new" disorder.

Progress: 102 completed questionnaires have been collected. Data is being analyzed and entered.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/89

STATUS: Completed

TITLE: Prevalence of Primary Measles Vaccine Failures in a Dependent Military Population and the Effect of MMR Revaccination on Antibody Response

START DATE: Nov 89

ESTIMATED COMPLETION DATE: Jan 91

PRINCIPAL INVESTIGATOR: COL Manuel Schydlower

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Bruce C. Velt, Ph.D.; MAJ Robert R. Wittler, MC; LTC Robert Martig, MS

KEY WORDS: Measles vaccine, MMR Revaccination, Antibody response

Study Objective:

- a. Determine the prevalence of primary vaccine failures.
- b. Assess risk factors in identifying primary vaccine failures.
- c. Determine the antibody response of measles seropositive and measles seronegative subjects to revaccination with MMR.

Technical Approach: All patients 6-20 years of age who wish to receive revaccination with MMR are eligible for the study. These individuals, and if applicable, their guardians will receive a printed explanation of the study. Informed consent concerning the collection of demographic and vaccination data and the risk of venipuncture will be obtained.

A data sheet with the date, subject's name, SSN, phone number, date of birth, date of prior MMR vaccination(s), ethnicity, and gender will be completed. Prior to being revaccinated, a venipuncture will be performed and a 5-7 ml of blood will be collected. The subject will then receive his/her MMR. A second venipuncture will be performed 2-3 weeks following MMR revaccination and 5-7 ml of blood will be collected. Specific measles IgG, IgM, and IgA will be determined by ELISA on each serum specimen. Subjects who are seronegative 2-3 weeks following revaccination will be asked to submit another specimen for antibody determination 6-8 weeks following revaccination.

There will be 500-700 subjects included in this study, and the duration of the study will be 4 months.

Relationships between prevalence of seropositivity, age, age of initial vaccination, interval between vaccinations, and mean DOD will be evaluated using stratified risk ratios, regression analysis and ANOVA.

Progress: The study has been completed and a paper has been accepted for publication in the November 1991 issue of Pediatrics.

Conclusion: The magnitude of increase in IgG titer following revaccination and analysis of trend for proportions of measles susceptible subjects were significantly related to the age of initial vaccination. This study supports continued routine measles revaccination. Additionally, revaccination appears to be of greater value at 11-12 years of age rather than at 4-6 years of age.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/20

STATUS: Completed

TITLE: DHEA Trends in a Population of Health Males

START DATE: Jan 90

ESTIMATED COMPLETION DATE: Dec 90

PRINCIPAL INVESTIGATOR: MAJ Rita L. Svec

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Michael A. Smutok, AMSC; LTC Molly Maguire, AMSC;
CPT Suzanne Cuda, MC

KEY WORDS: DHEA trends

Study Objective: To define the following variables in a population of healthy males: DHEAS, Insulin/glucose ration, % body fat, cholesterol, and lipid profile in an effort to define subgroups to use for a secondary study of the predictors for sudden cardiac death.

Technical Approach: Exclusion Criteria: Actively attempting weight loss, taking antihypertensives or psychotropic medications. Number of subjects: 150 - 40% are smokers. Type of subjects: Men entering the SMA January 1990 class. Laboratory procedures used: During the routine venipuncture for health risk appraisal, an extra 10cc tube will be drawn for our studies. Blood will be aliquotted and frozen for later assay for insulin, DHEAS and lipid profiles. Duration: This is a single blood draw, which will be compared to the SMA health risk appraisal questionnaire, and % body fat measurement already being performed as part of the routine for entrance into the SMA. Data analysis: Comparisons will be made between groups subdivided by age, comparing DHEA, % body fat, and insulin glucose ratios. We hope to be able to subdivide the groups into low risk, moderate risk and high risk, based on these preliminary data, and use these criteria in later studies. Statistical correlation using Analysis of Covariance, and Linear Regression Analysis will be used.

Risk to subject: 10 cc of blood loss, which is inconsequential. Participants are already having a venipuncture for health risk appraisal. Potential benefit: Subjects will be informed if their data places them in a potentially higher risk group for sudden cardiac death.

Progress: 200 health males underwent blood testing for DHEA-sulfate and insulin and lipid profiles. We were looking for trends in DHEA-sulfate and smoking and lipid profiles. No trends were found. There was no correlation between DHEAS and weight or insulin and weight.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/59

STATUS: Ongoing

TITLE: Emergency Use of Recombinate in Patient with Hemophilia A, Factor VIII Deficiency

START DATE: Sep 91

ESTIMATED COMPLETION DATE: Nov 91

PRINCIPAL INVESTIGATOR: Dr. Jerry J. Swaney

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Hemophilia

Study Objective: To use recombinant DNA Factor VIII (Recombinate) to avoid exposure to any contaminants since this is a pure synthetic product.

Technical Approach: Patient is a 5 month old male newly diagnosed with Hemophilia A, Factor VIII deficiency who has not required any replacement factor infusion to control bleeding. The emergency IND was requested to have Recombinate available until a formal IND is procured. Drug will be obtained from Baster Healthcare Corporation (Hyland Division) through the Regional Hemophilia Center, Univ of Texas Health Science Center at Houston. Recombinate will be administered in accordance with drug company protocol.

Progress: Because of questions regarding initial Factor VIII level, parents are considering if they wish to be on the study. Protocol will be terminated if parents decline participation.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/62

STATUS: Ongoing

TITLE: Medical Experience of The Third Armored Cavalry Regiment During Operations Desert Shield and Desert Storm

START DATE: Aug 91

ESTIMATED COMPLETION DATE: Nov 91

PRINCIPAL INVESTIGATOR: MAJ Glenn M. Wasserman

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Brian Martin MC (FAMC); CPT Howard Oaks MC; MAJ Harold McAdoo DC; CW2 Richard Harvey (3ACR PA); CDR Bruce Merrill (NAMRU III); CDR Craig Hyams (NMRI)

KEY WORDS: Medical experience, ODS

Study Objective: The aim of this project is to review and analyze the military, medical experience of first and second echelon medical units attached to a forward line unit (The Third Armored Cavalry Regiment) during Operations Desert Shield and Desert Storm.

Technical Approach: Data will be obtained primarily from retrospective review of preventive medicine disease surveillance data, self-completed questionnaires (Fourth Squadron), stool culture and ova & parasite analysis, and after action reports. There will also be anecdotal reports and data from the medical troop commander, dentist, acting psychiatrist and a physician assistant.

Progress: Study just begun. Data is being correlated.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/88

STATUS: Ongoing

TITLE: Incidence of *Corynebacterium Haemolyticum* Pharyngitis in an Adolescent Clinic

START DATE: Oct 89

ESTIMATED COMPLETION DATE: Sep 93

PRINCIPAL INVESTIGATOR: MAJ Martin Weisse

DEPARTMENT: Ped

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: *Corynebacterium Haemolyticum* Pharyngitis, Adolescents

Study Objective: The incidence and seasonal variation of *corynebacterium haemolyticum* pharyngitis will be determined over a one year period in the Adolescent Clinic at WBAMC.

Technical Approach: All patients (13-20 years of age) presenting to the Adolescent Clinic at WBAMC with a complaint of "sore throat" who receive a throat culture will automatically be included in the study. It will be conducted over a one year period. A checklist of associated signs and symptoms will be used to standardize the information charted on each patient. No additional tests are needed. The throat culturette which would be obtained anyway will be sufficient. In the lab, the culturette will be plated out on the usual blood agar plates, but those from the Adolescent will be marked to be held for 72 hours. Group A beta hemolytic strep can be read at 24 hours (or less), but *corynebacterium haemolyticum* takes 48-72 hours for adequate growth. Those plates with growth suspicious for *Corynebacterium haemolyticum* will be verified using sugar fermentation techniques.

Patients with a positive culture will be contacted and prescribed a ten day course of erythromycin. (The lab will do sensitivity tests periodically on cultures to determine alternate therapies.) The patients will also be requested to return after treatment for a follow-up throat culture to ascertain eradication of infection. Those who have not responded will be tested for co-incident infectious mononucleosis. Household contacts under age 22 will be requested to also have a throat culture (due to the high incidence of positive results in this population shown in Miller's study).

Those patients identified as having *corynebacterium haemolyticum* will benefit by treatment which should decrease duration of illness, recurrence of infection, and propagation to others in the household. Risks are minimal. No invasive tests are being done. Erythromycin (250mg four times a day for ten days) is among the safest of antibiotics. (Its main side effect is nausea, which can be minimized by taking it with food.)

Progress: Drs. Martinko and Imai have left this facility. Dr. Martin Weisse will assume the role of PI and continue the project.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/52

STATUS: Completed

TITLE: The Impact of Special Pay on Army Physician Retention

START DATE: Jul 90

ESTIMATED COMPLETION DATE: Mar 91

PRINCIPAL INVESTIGATOR: CPT Kim C. Strunz

DEPARTMENT: Pers

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Susan A. MacManus, Ph.D.

KEY WORDS: Special pay, Physician retention

Study Objective: Test the following hypotheses:

1. The larger the total amount of special pay a physician receives, the more likely he/she is to cite it as a major reason for remaining in the Army rather than going into private practice.
2. The greater the number of different types of special pay a physician receives, the more likely he/she is to cite special pay as a major reason for remaining in the Army rather than going into private practice.
3. Special pay is more likely to be cited as a major reason for remaining in the Army by physicians assigned to a medical facility in the U.S. than by physicians assigned to a medical facility in a foreign country.

Technical Approach: The study will be based on survey data generated through a mail questionnaire with one follow-up contact of those not responding to the first request by the suspense date. The survey will be distributed to the universe of Army physicians assigned to WBAMC as of 27 June, 1990. A number of different types of statistical analytic techniques, ranging from simple percentage distributions to contingency table analysis, discriminant function analysis, and other relevant techniques, will be utilized. The variables are a mixture of nominal-, ordinal-, and interval-level measures, necessitating a wide range of analytic techniques.

Progress: This project was completed. Results show that in spite of significant increases in total compensation (base pay + special pay), few physicians regard it as a reason, or the most important reason, for remaining on active duty. Only 18.6% of WBAMC physicians and 12.9% of 18th MEDCOM physicians cited this reason. For both groups, total compensation ranks behind obligation due to medical school/training, service to country, overall job satisfaction, family/personal reasons, retirement benefits, and working hours. For 18th MEDCOM physicians, total compensation also ranks behind medical education benefits and travel opportunities and is equal to avoiding the cost of office equipment and personnel. Two papers were generated from this study. One was accepted for publication in the Public Administration Quarterly. The other was presented at the Southwestern Political Science Association Annual Meeting in San Antonio (Mar 91) and was also submitted for publication to Social Science Quarterly (special issue on the military).

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/23

STATUS: Ongoing

TITLE: Evaluation of HBV Immunization Using a Series of Two Heptavax and One Recombivax

START DATE: Mar 90

ESTIMATED COMPLETION DATE: Jan 92

PRINCIPAL INVESTIGATOR: Karlyn Pearl

DEPARTMENT: PrevMed

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Ana Ortiz, MC; CPT Carl Gibson, MC

KEY WORDS: HBV Immunization

Study Objective: To evaluate if completing the immunization process of active duty personnel with Recombivax after they have received their first two doses with Heptavax will increase their hepatitis surface antibody titers to levels similar to those receiving the conventional three doses of Heptavax. In addition, will like to find out if their titers are similar a year later.

Technical Approach:

Group A - Control: Fifty patients who have received two doses of Heptavax and are ready to receive the third dose (6 months since their first vaccine, and 5 months post the second vaccine) will be studied. Blood for hepatitis surface antibodies will be obtained at the time of their third immunization, three weeks later, and a year later.

Group B - Study Group: Fifty patients who had received the second dose of Heptavax and are ready to receive their third dose (Recombivax) will be studied. Blood for Hepatitis-S antibodies will be obtained at the time the third vaccine is due, three weeks later, and a year later. These patients will be receiving Recombivax.

Patients will be selected to participate in the study group as follows. As patients present to receive either the Heptavax or the Recombivax, every other one will be asked to participate in the study.

Progress: Mrs. Pearl assumed PI responsibility due to COL Ortiz' PCS. Study was initiated with 50 controls and 50 study participants (total 100). At the 6-week interval, 98 of the 100 were contacted and blood drawn. At the 1-year interval, 40 participants were lost due to Operation Desert Storm, PCS moves, retirements and inability to locate, leaving 60 participants. We are in the process of having RAI evaluate the remaining blood specimens for the 60 participants at this 1-year interval.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/10

STATUS: Ongoing

TITLE: Assessment of Risk Factors for HIV Infections Among Active Duty U.S. Army Personnel with Documented Recent HIV-Antibody Seroconversion

START DATE: Feb 91

ESTIMATED COMPLETION DATE: Feb 93

PRINCIPAL INVESTIGATOR: Karlyn K. Pearl

DEPARTMENT: PrevMed

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Arthur R. Morton; Henry Rodriguez

KEY WORDS: HIV seroconversion

Study Objective: To assess demographic and behavioral determinants associated with new HIV infections. Incident cases are the only population which allow us to investigate important features of the current HIV infection epidemic. Risk factors and their relative significance as determinants of HIV infection will be assessed by comparing medical, demographic, and behavioral histories of active duty personnel recently infected with HIV with histories of individuals who have not seroconverted over a similar time period.

Technical Approach: The study will be conducted using a case-control design. A case will be defined on the basis of HIV-Ab seroconversion (positive Western blot in duplicate). Controls will be randomly selected HIV-Ab negative active duty personnel at the same posts where cases occur, and will be matched to each case on: Age (+/- 2 yrs), race/ethnicity, grade category (junior enlisted, senior enlisted, officer), and length of service in the Army. Two controls will be recruited for each case. Controls must have been tested negative for HIV-AB no earlier than three months before the positive test date of their matched case. Based upon standard methods for determining required sample sizes in a case-control study and the expected number of HIV-AB seroconverters, a 2-year study period is anticipated. All active duty personnel with confirmed HIV-Ab seroconversion will be eligible for inclusion in this study. Cases will be identified each month by review of the USAHDS data base. Physicians in charge of the HIV testing and evaluation programs at posts from which cases are reported will be contacted by WRAIR and asked to invite incident cases to participate in this study. This study is designed to ensure strict confidentiality. All links between name, social security number, or other identification and study numbers are destroyed after the interviews are completed at the study site.

Progress: Study progress was undermined by troop deployment (Desert Storm) and a 4-month staffing shortage at the City County Health Department. With the return of the troops and resolution of the staffing shortage, enrollment will continue.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 87/71

STATUS: Ongoing

TITLE: Emergency Procedures Laboratory (Carpine Model)

START DATE: Jul 87

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: CPT Michael Peterson

DEPARTMENT: DPCCM

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Emergency procedures laboratory

Study Objective: To train accredited physicians who are not dealing with emergencies on a day-to-day basis, but may be called upon to perform this function. The goat model will simulate the human emergency patient.

Technical Approach: Cricothyroidotomy, venous cutdown, chest trauma management, and peritoneal lavage procedures will be accomplished in accordance with training manuals for each procedure.

Progress: No training sessions were conducted in the past year. Protocol will be updated to appropriate format.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 88/02

STATUS: Terminated

TITLE: Surgical Stapling Procedures Laboratory (In Dogs)

START DATE: Jun 1988

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: LTC Warren F. Bowland

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Stapling

Study Objective: To train accredited attending physicians and residents in the use of automatic suturing devices including their applications and limitations in a laboratory environment before they are called upon to use these instruments in human surgery.

Technical Approach:

I. Gastrointestinal Applications Procedures

- a. Splenectomy
- b. Hemigastrectomy w/Billroth II Reconstruction or Hemigastrectomy w/Billroth I Reconstruction
- c. Small Bowel Resection w/Functional End-to-End Anastomosis

II. Other Abdominal Applications

- a. Nephrectomy
- b. Large/Small bowel Resection w/End-to-End Anastomosis by Triangulation

III. Closure

- a. Fascial Closure Techniques
- b. Skin Closure Techniques

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: This protocol was replaced with WBAMC #91/13 which utilizes the porcine model.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 88/59

STATUS: Ongoing

TITLE: Animal Model (Ovine) Laboratory, Advanced Trauma Life Support Course (ATLS)

START DATE: Jun 1988

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: LTC Warren F. Bowland

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Steve Carey, MC

KEY WORDS: Trauma

Study Objective: To train accredited physicians who are not dealing with major trauma on a day-to-day basis, but may be called upon to perform this function. The goat model will simulate human trauma.

Technical Approach: Animal Procedures: Cricothyroidotomy; Venous Cutdown; Chest Trauma Management including needle decompression, tube thoracostomy and pericardiocentesis; and Peritoneal Lavage
Training manuals will be used for each training procedure.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: The ATLS course is part of the training for physicians at WBAMC. Eighteen sheep were utilized. Approximately 80 physicians were trained under this protocol during this fiscal year.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/42

STATUS: Ongoing

TITLE: Fiberoptic Endoscope Cholecystectomy in the Porcine Model

START DATE: Oct 90

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: LTC Warren Bowland

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Stephen Carey, MC; CPT Anthony J. Canfield, MC; CPT Dennis Eastman, MC; CPT Steve Bodney, MC.

KEY WORDS: Fiberoptic Endoscope Cholecystectomy

Study Objective: To determine feasibility of conducting cholecystectomies at WBAMC with endoscopic equipment rather than a laparoscope. Thpericardiocentesis; and Peritoneal Lavage
Training manuals will be used for each training procedure.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: The ATLS course is part of the training for physicians at WBAMC. Eighteen sheep were utilized. Approximately 80 physicians were trained under this protocol during this fiscal year.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/15

STATUS: Ongoing

TITLE: Certification Training: Advanced General Surgery Laser Laparoscopic Procedures in the Porcine Model

START DATE: Apr 91

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Warren Bowland

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Lawrence Runke

KEY WORDS: Laser laparoscopy training

Study Objective: To provide training and certification of General Surgery Surgeons in laser laparoscopic cholecystectomy, hernia repair, and appendectomy. This training will enable them to develop the proficiency required to perform these operative procedures in human patients.

Technical Approach: The animals' food will be withheld for a period of 18 hours prior to surgery. The pigs' hair will be clipped from the abdomen. The animals will be placed in dorsal recumbency. After the skin is prepped, an insufflation needle will be inserted and the abdomen will be filled and maintained with 15 mm Hg pressure of CO₂. A trocar/cannula will be placed near the umbilicus for introduction of the video laparoscope which will enable monitoring of the procedure on a video screen. Two to three additional trocars/cannulas will be placed for introduction of laparoscopic graspers, scissors, laser fibers, etc. The cystic duct and artery will be bluntly dissected free, double ligated or clipped, and transected. The gallbladder will be dissected free from the liver bed by sharp, blunt, electrosurgical and laser techniques. Once free from hepatic parenchyma, the gallbladder will be approximated to the body wall, decompressed and pulled through one of the central trocar puncture sites.

Other advanced laparoscopic procedures will include hernia repair and appendectomy. Laparoscopic cannulas will be repositioned as necessary for subsequent procedures to enable visualization and tissue manipulation. Hernia repair: A defect will be created in the internal inguinal ring by sharp and blunt technique. Subsequently, the created hernia will be repaired by laparoscopic suture and stapling techniques. Appendectomy: The distal cecum will be isolated and mobilized. The distal segment will then be resected and closed by laparoscopic suture and stapling techniques. The appendage will be approximated to the body wall with large graspers and removed through a central puncture site.

Training is scheduled for six (6) WBAMC surgeons and ten (10) Sierra surgeons.

Amendment (AUC Approved Apr 91) increased the number of training sessions, animal requirements and resource requirements to accommodate training of 32 physicians.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Twenty-seven animals have been used. Training is conducted in strict compliance with protocol guidelines.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/37

STATUS: Ongoing

TITLE: Certification Training: Lasers in Urology in the Porcine Model

START DATE: Jun 91

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Warren Bowland

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Fernando L. Diaz-Ball

KEY WORDS: Laser training, Urology

Study Objective: To provide training and certification of Urological Surgeons in laser cystoscopic procedures. This training will enable them to develop the proficiency required to perform these operative procedures in human patients.

Technical Approach: The animals' food will be withheld for a period of 18 hours prior to surgery. The pigs' hair will be clipped from the abdomen. The animals will be placed in dorsal recumbency. **Surgical Procedure:** A cystoscope will be introduced through the urethra into the urinary bladder. Methylene blue 2% in N saline will be infused in to various regions of the urinary bladder mucosa for training with the ND:YAG laser and other lasers, such as the CO₂, Argon, or KTP. Laser surgery training will include techniques from the external urethral os to the urinary bladder and possibly the ureters. If difficulty is encountered with introduction of the cystoscopy via the urethra (since the urethral os is up to 4 cms inside the vagina, anteriorly) the urinary bladder will be exposed by laparotomy via a mid anterior suprapubic abdominal incision. Urethral laser procedures can then be conducted by retrograding the cystoscope through the bladder neck. If larger vesicular tumors are required for laser excision or vaporization training, segments of the rectus muscle will transplanted into the bladder mucosa acutely. The bladder will then be closed with 3-0 dextron. Training is scheduled for a maximum of six (6) WBAMC surgeons and ten (10) Sierra surgeons.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: No training was conducted.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/38

STATUS: Ongoing

TITLE: Certification Training: Lasers in Pulmonary and Otolaryngology in the Ovine Model

START DATE: Jul 91

ESTIMATED COMPLETION DATE: Nov 91

PRINCIPAL INVESTIGATOR: COL Warren Bowland

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Miller F. Rhodes

KEY WORDS: Laser training, Pulmonary; Laser training, Otolaryngology

Study Objective: To provide training and certification of pulmonary/ENT surgeons in laser laryngoscopy, bronchoscopy, and esophagoscopy procedures. This training will enable them to develop the proficiency required to perform these operative procedures in human patients.

Technical Approach: The animals' food will be withheld for a period of 24 hours prior to surgery. Wool will be sheared from the neck and cranial thorax. The sheep will be placed in dorsal recumbency.

Simulated tumor implantation: A 5cm vertical incision will be made at the level of the cricothyroid membrane. A small segment of sternothyroid muscle will be resected and transplanted through the cricothyroid membrane to simulate a laryngeal tumor. Sternothyroid muscle will also be resected and transplanted into the esophageal lumen via a 1cm incision in the esophageal wall to simulate esophageal tumors. The tracheal and esophageal incisions will be closed with 3-0 dextron. Procedures will be repeated as necessary to simulate additional tumors for excision training.

Tumor excision: An endoscope will be inserted through the mouth into the airway or the esophagus depending on the training procedure. A laser fiber will be inserted through the endoscope channel and use in training in tumor excision or vaporization with the ND:YAG laser and other lasers, such as the CO₂ or KTP, if available.

Training is scheduled for a maximum of six (6) WBAMC surgeons and ten (10) Sierra surgeons.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: One course was conducted in Jul 91 and 6 physicians were trained. A second course is planned for Nov 91. Training was conducted in strict compliance with protocol guidelines.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/12

STATUS: Ongoing

TITLE: Combat Trauma Surgery Using a Portable contact Nd-(YAG) Laser

START DATE: Feb 89

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: CPT Anthony J. Canfield

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL John McPhail, MC; CPT Michael J. Snyder, MC; MAJ Steven Carey, MC

KEY WORDS: Laser training, Surgery

Study Objective: The main purpose of this laboratory will be to train physicians who are involved in the care of trauma victims, in the use of the Neodymium (Nd):YAG laser in surgery, and to familiarize them with the laser's applications in trauma management.

Technical Approach: Prior to the actual experiments, each participant in the protocol will be instructed in the safety precautions and the proper use of the (Nd)-YAG laser. Two animals will be used to demonstrate proper technique to the surgeons participating. After proper instruction, two surgeons and one to two assistants will perform the procedures on each animal, allowing each surgeon to be the primary surgeon on two operations.

The actual operations will proceed as follows: Each animal will undergo one survival and one non-survival abdominal surgical procedure. After the animal is adequately anesthetized (see alleviation of pain and distress below), IV lines and EKG monitors will be placed. A midline abdominal incision will be made and a brief exploration of the abdomen will be performed. A segment of the liver will then be injured with a combination of blunt and sharp trauma so as to cause injury deep into the parenchyma of the tissue. At this point, the (Nd)-YAG laser will be used to obtain hemostasis via a combination of resection and coagulation techniques. After appropriate repair of the liver, similar injuries to the pancreas, spleen, kidney, and intestines will be produced. Each injury will be repaired using the (Nd)-YAG Laser. No more than 50% of the liver parenchyma, or the parenchyma of the other abdominal organs will be injured during the operation. After appropriate hemostasis is obtained, the abdomen will be closed with a standard 3 layer closure, and the animal will be allowed to recover from general anesthesia. The animals will be managed as described below in the post operative care plan.

Each animal will be allowed to recover 1-2 weeks from the initial surgery prior to the second operation. At this surgery the abdomen will be entered in similar fashion and explored. The healing of the liver, pancreas, spleen, kidney, and intestinal repair sites will be assessed by the operating team for the following items: 1 Hemostasis, 2 tissue necrosis, 3 and evidence of any injury to surrounding organs and tissue. After evaluation of the intra-abdominal healing, a similar procedure will be performed on other segments of the above named organs, as described above, and the repair will be made using the (Nd)-YAG laser. At the conclusion of the surgery the animal will then be euthanatized according to the protocol listed below. At no time during the operation or the recovery time will the animal be allowed to suffer, and if appropriate alleviation of pain can not be achieved, the animal will be euthanatized.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: No animals were used as training models during 1991 due to the conduct of collaborative training with Sierra Medical Center and postponement of the animal WBAMC laser training until Nov 91.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/31

STATUS: Completed

TITLE: Combat Trauma surgery Using a Portable contact Nd-(YAG) Laser in the Porcine and Ovine Models

START DATE: Apr 89

ESTIMATED COMPLETION DATE: Feb 91

PRINCIPAL INVESTIGATOR: CPT Anthony J. Canfield

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL John F. McPhail, III, MC

KEY WORDS: Laser visceral surgery

Study Objective: Compare the use of the Nd-(YAG) to conventional surgical techniques, with respect to blood loss and operative time. Actually test this laser in a field environment using an animal model in a F.A.S.T. unit with a wartime casualty scenario. Determine if advanced surgical techniques using a new portable contact Nd-(YAG) laser can be realistically and effectively used in a field surgical unit.

Technical Approach: PHASE I: Comparison of ND:YAG Laser Trauma Surgery Repair to Conventional Repair Techniques.

(a) This study will be comprised of two animal groups of ten swine each: GROUP A- Solid visceral trauma repaired with the ND:YAG laser; GROUP B- Solid visceral trauma repaired by conventional means. The following parameters will be measured immediately before and after the initial surgery, prior to the evaluation by exploratory laparotomy, and at other times as clinically indicated: Complete blood counts, chemistries (SMA 22), body weight. During the surgical procedures, physiological parameters (heart rate, arterial pressure, and body temperature) will be measured at 15 minute intervals. All data will be utilized for chronological comparisons to determine immediate post operative blood loss and to follow changes from baseline during the recovery period.

(b) Surgeries will be conducted in the operating room of building 7776 and observed in the recovery room for 24 hours prior to returning to the routine housing. After an appropriate level of anesthesia is reached, all animals will be instrumented with a femoral arterial pressure line, an electrocardiogram, and a body temperature probe. A left paramedian incision will be made and a standardized traumatic lesion will be made in the liver, spleen and left kidney. This will be accomplished under laparoscopic visualization with a fabricated instrument which will produce both sharp and blunt visceral trauma (see figure 1). This will ensure uniformity of the injuries to each organ, so that the surgical repair of the injuries can be objectively compared. After the injuries are created, the left paramedian incision will be closed. The repair of the injuries will begin after 15 minutes have elapsed from the wounding of the first organ, and a stopwatch will be started to measure the time from the midline abdominal incision to the completion of the 3 layer closure.

(c) Animals will be selected for either laser or conventional repair at random. The procedures will also be completed in blocks such that the procedures are completed in one animal from each group before continuing to the next block of experimental animals. The injuries in each animal will be identical, regardless of the group to which it will be assigned. A staff surgeon and a resident surgeon will comprise the surgical team, and this team will perform all the procedures in both Group A and Group B. This will eliminate the variability from surgeon to surgeon, and allow assessment of improved skill with experience. The surgeons that will be assigned to this surgical team are Dr. John F. McPhail, Chief, Department of Surgery, Dr. Stephen Carey, Chief of Trauma Surgery, and Dr. Anthony J. Canfield, Surgical Resident.

(d) Two weeks following the initial surgery the animals will be re-explored to assess healing. Gross examination of the organs and surrounding tissues will be made and tissue from each repair site will be excised and submitted for histopathological examination. Statistical analysis of the data obtained will be performed to determine the quality and speed of both Laser and Conventional repair techniques.

PHASE II- Field Testing Exercise: The field exercises (FTX) will be conducted in early September. It is anticipated that the FTX will be conducted over a two day period and will require approximately 8 sheep per day. A new group of participants will attend the exercise each day in order to maintain adequately staffed duty positions. Animals will be anesthetized as stated below and surgically traumatized prior to the exercise. The physicians will be required to triage patients and conduct emergency care procedures taught in Advance Trauma Life Support Courses. In addition they will also utilize the laser unit to verify effectiveness compared to conventional means. All animals will be euthanatized as stated below following the surgical procedures.

ADDENDUM: Prior to induction of surgical injury to the liver, spleen, and kidney, heparin 50 U/kg will be infused intravenously. This degree of heparinization will produce more severe hemorrhage for both the laser and the conventional repair groups.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in Item 5.b. (Animal Procedures).

Progress: The study was completed and a paper written. Twenty animals were used; four were withdrawn due to early problems in determining blood loss.

Results: Conventional and laser repair of liver and spleen injuries were compared in a controlled study using the porcine model. Sixteen pigs were randomly placed in either the laser or conventional group. The injuries were made with a stellate clamp, producing a standardized injury in both the liver and the spleen. The laser repair was performed with a Nd(YAG) laser, using non-contact technique and also with a new through-glass compression technique not yet described. Operative time, blood pressure, weight change, hematocrit change, depth of liver necrosis, and blood loss were measured. The operative time ($p < 0.01$), and the drop in hematocrit were significantly less in the laser group ($p < 0.01$). The depth of necrosis was the same for both groups. The laser techniques provided faster repair of liver and spleen injuries with less blood loss. Laser may have an application in repair of traumatic injuries.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/70

STATUS: Ongoing

TITLE: Tracheal Reconstruction with Synthetic Gore-Tex Grafts in the Rabbit Model

START DATE: Nov 90

ESTIMATED COMPLETION DATE: Nov 91

PRINCIPAL INVESTIGATOR: CPT Anthony J. Canfield

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Miller F. Rhodes, MC; LTC Troy Reyna, MC

KEY WORDS: Tracheal reconstruction, Tracheal prosthesis

Study Objective: To identify a tracheal prosthesis material and surgical technique which may be suitable for reconstruction of the human trachea.

Technical Approach: This study will be conducted in two phases. Phase I will be to determine the maximum graft length allowing successful tracheal reconstruction; Phase II will be designed to determine the minimum interval for subcutaneous implantation required to have successful tracheal reconstruction.

In both Phase I and II the grafts will be implanted in two stages. The first stage will consist of implantation of the Gore-Tex prosthesis in the subcutaneous tissue with a silastic stent to keep the lumen patent and induce fibrous capsule formation. The animals will then be recovered from anesthesia and monitored for a prescribed period of time. The second stage will consist of harvesting the graft, after an appropriate amount of time is allowed for ingrowth of fibrous tissue, and replacing a segment of trachea with the graft. The animals will then be recovered and observed over a period of three weeks time while receiving prophylactic antibiotics.

Initially, two animals will be used to develop the technique and verify suitability of the rabbit as a model. The graft length for these animals will be 1 cm for each rabbit. The graft will remain in the subcutaneous pouch for three weeks prior to the tracheal reconstruction. Three weeks following the tracheal reconstruction, the rabbits will be evaluated to verify patency, infection rates, and degree of re-epithelization in the following manner: The animals will be anesthetized with spontaneous ventilation occurring. Utilizing telescopic bronchoscopy the lumen will be inspected for stenosis. The animal will be euthanatized and the graft cultured and histologically examined for infection and tissue morphology, respectively.

If the outcome of the pilot is successful and the model appears to be appropriate, then the study will proceed as follows:

PHASE I: Rabbits will be divided into four groups of six rabbits each:

Group I (3cm prosthesis length)

Group II (4cm prosthesis length)

Group III (5cm prosthesis length)

Group IV (6cm prosthesis length)

The grafts in these animals will be evaluated at intervals of 4 days, 1 week, 3 weeks, 6 weeks, 9 weeks, and 12 weeks. The evaluation will consist of direct laryngoscopy and bronchoscopy with video recording of the procedure and computer analysis of the dynamic change in lumen size with inspiration and expiration.

Criteria for a failed graft will be 30% obstruction of the resting lumen size or a dynamic decrease to 30% of the lumen diameter with respiratory movement. Brush biopsies of the luminal surface will be taken for bacterial culture and for microscopic evaluation of lumen epithelium.

All surgical and bronchoscopy procedures will be conducted only after animals are appropriately anesthetized as stated below. If unable to prevent animal pain or suffering following procedures, the respective rabbits will be euthanatized according to methods stated below. Any animals that die or are euthanatized prior

to the termination of the experiment will be necropsied to determine the cause of death, if applicable, and to evaluate the graft sites grossly and microscopically.

With the exception of 8 long term animals, all remaining animals will be euthanatized 12 weeks following the tracheal reconstruction. The grafts will then be excised and examined grossly and microscopically. Two of the remaining animals from each group will be observed for a total of 6 months to determine if any long term complications occur.

PHASE II: After determination of the maximum graft length allowing successful reconstruction, the interval between subcutaneous implantation and transfer of the graft for tracheal reconstruction will be evaluated. On this basis the minimal allowable time between subcutaneous transplantation of the Gore-Tex graft and the tracheal reconstruction can be determined. This will be the final phase of the study as planned. Four groups of six animals each will be required. The graft will be implanted as described in Phase I.

Grafts will be harvested as follows: Group I - one week; Group II - two weeks; Group III - three weeks; and Group IV - four weeks. Following harvesting of the PTFE graft and tracheal reconstruction, each group of animals will undergo evaluation as described in Phase I.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: A total of eight pilot animals have been entered into the study. Antibiotic associated enterocolitis occurred in three of the animals and antibiotic regimens have been altered and shortened. The surgical technique is now established and as long as airway infections are minimized due to the two stage pouch technique and the use of Iodoform drapes, the experimental portion of the study should begin during the 1st Qtr, FY 92.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/41

STATUS: Terminated

TITLE: Intestinal Anastomosis with an Interpositional Absorbable Stent and a Neodymium (Nd): YAG Laser in the Rabbit Model

START DATE: Indefinite

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: CPT Anthony J. Canfield

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: John F. McPhail, COL, MC; Stephen Carey, MAJ, MC; Ann Price, CPT, MC

KEY WORDS: Laser, intestinal anastomosis

Study Objectives:

1. Demonstrate the ability to weld an end-to-end intestinal anastomosis utilizing a ND:YAG laser and an absorbable stent.
2. Test the strength of the intestinal anastomosis after different periods of healing.
3. Evaluate the long term healing of the intestinal anastomosis.

Technical Approach: INITIAL PHASE: Four rabbits will be used initially to evaluate the procedure and refine the technique. The small bowel will be transected in two locations in each of the four rabbits. One of the anastomosis will be performed with the laser technology described above and the other by conventional suturing techniques. This will provide a laser and conventional anastomosis in each animal for easy comparison. Two rabbits will be assigned to each group to allow evaluation of the surgical sites on days 4 and 10 post surgical. Gross appearance will be recorded and bursting strength will be measured with a standard manometer. Techniques will be assessed and, if necessary, minor modifications to the procedures will be made prior to the start of the main phase.

MAIN PHASE: Sixty rabbits will be randomly assigned to one of four groups of 15 rabbits each:

Group 1 will receive a laser anastomosis and a conventional anastomosis at 15 and 30 cm from the ligament of treitz. They will be recovered for 15 days post-anastomosis. At this time, ten of the rabbits will be re-explored surgically and the anastomoses will be photographed, evaluated for evidence of leakage, and then tested for bursting strength. These animals will then be euthanatized as outlined below. The other five animals from this group will be euthanatized and necropsied.

Group 2 will receive anastomoses in the identical manner to group 1, but will be re-explored or necropsied at 30 days post-anastomosis. The same manner of evaluation will be used as for group 1.

Group 3 will receive anastomoses in the identical manner to group 1, but will be re-explored or necropsied at 60 days post-anastomosis. Evaluation will be the same as for groups 1 and 2.

Group 4 will receive anastomoses in the identical manner to group 1, but will be re-explored or necropsied at 60 days post-anastomosis. Evaluation will be the same as for groups 1 and 2 and 3.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Project cancelled in Apr 91. Laser Surge Inc. is no longer seeking FDA approval for their intestinal anastomosis stent/laser system. They have dropped the line entirely and the system is no longer available for procurement and testing.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/01

STATUS: Ongoing

TITLE: The Effect of Fibrin Sealant on Skin Graft Inhibition of Wound Contraction in the Porcine Model

START DATE: Nov 90

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: CPT Gary R. Culbertson

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Julio Ortiz

KEY WORDS: Adhesive tissue, Wound healing, Fibrin sealant

Study Objective: Our objective is to determine if fibrin sealant fixation of skin grafts augments their ability to inhibit wound contracture in the porcine model. Theoretically, if the fibrin sealant fixation of skin grafts allows for the inhibition of wound contracture in the animal model, this could be applied to the human patient in a later study.

Technical Approach: Six domestic swine will be utilized. Prior to each surgical procedure, anesthesia will be induced and surgical sites will be prepped. During surgery, four pairs of full thickness skin grafts will be made. A comparison of graft contracture of fibrin sealant treated grafts versus untreated grafts will be made between each pair of wounds. Graft site areas will be quantified every three days postop to day 28 using standardized photography or video digitization into a computer graphics program for analysis. For a period of 48 hours after recovery, the animals will be caged individually and allowed free access to food and water. Afterwards, they will be group housed. Evaluations will not be conducted on wounds showing evidence of infection, excessive hemorrhage or poor coaptations. The surface area of each original graft at day zero will be considered 100% and subsequent determinations will be reported as a percentage of the initial size. Contraction rates of each group will be compared statistically.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Additional funding was requested and approved to allow measurements to be made on the enstronge unit at Texas Tech. When all the equipment and chemicals have been gathered and PI is granted time, the protocol will begin.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/02

STATUS: Ongoing

TITLE: The Effect of Fibrin Sealant on Breaking Strength of Incisional Wounds in the Porcine Model

START DATE: Nov 90

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: CPT Gary R. Culbertson

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Julio E. Ortiz; LTC Phillip L. Day

KEY WORDS: Fibrin sealant

Study Objective: To determine if fibrin sealant enhances wound healing as evaluated by wound breaking strength and histological evaluation of tissue in the animal model (i.e., fibroblast proliferation, angiogenesis, etc.). Should fibrin sealant prove efficacious in the animal model to promote wound healing, this could be utilized in the human patient in a comparative study to evaluate wound healing and thus promote the strength of the wound.

Technical Approach: Six domestic swine will be utilized. Prior to each surgical procedure, anesthesia will be induced and surgical sites will be prepped. During the initial surgery, four pairs of surgical incisions will be made. A comparison of fibrin sealant versus normal healing will be made between each pair of wounds. One pair of wounds will be harvested from each animal at day 7, 14, 21, and 28 post wounding. Breaking strengths and histological analysis of paired wounds will be determined. For a period of 48 hours after recovery, the animals will be caged individually and allowed free access to food and water. Afterwards, they will be housed together. Evaluations will not be conducted on wounds showing evidence of infection, excessive hemorrhage or poor coaptations. Adhesiveness of each group will be compared statistically.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Additional funding has been requested and approved to allow measurements to be made on the enstronge unit at Texas Tech. Once all the equipment and chemicals have been acquired and the PI is granted research time, the protocol will begin.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/26

STATUS: Ongoing

TITLE: Artificial Substitutes for the Urinary Bladder in the Porcine Model

START DATE: May 90

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Fernando Diaz-Ball

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Leonard Maldonado, MC; Chief Resident, General Surgery

KEY WORDS: Bladder Substitute, Continent Urinary Diversion

Study Objective: Our objective is to provide training in a variety of techniques previously described in the literature for fashioning a bladder substitute from autologous bowel. Our experience with this will enable us to perform these operations in our patient population. The ongoing nature of the protocol is necessary to maintain technical proficiency and add refinements.

Technical Approach: No surgical procedures will be conducted without the administration of general anesthesia. Anesthesia will be administered and monitored by veterinary staff assigned at Biological Research Service.

The Urology Clinic attending staff will devote 1-2 days each month to performing previously agreed upon continent urinary reservoir procedures. These include Mainz Pouch, Koch Pouch, and Indiana Reservoir. The common denominator of the various procedures is that autologous bowel is fashioned into a urinary reservoir out of continuity from the fecal stream. This reservoir is then anastomosed to the urethra or to a continent catheterizable stoma.

The proposed model is the porcine. We elected to euthanize the animals at the end of the surgical procedure prior to recovery from anesthesia. In the future, we may choose to request an amendment allowing us to do survival studies as long as animal suffering can be prevented.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in Item 5.b. (Animal Procedures).

Progress: This training protocol is used to review the finer details of technique prior to actual performance of human surgery. Another session will be conducted in preparation for two human radical cystoprostatectomies scheduled for early FY92.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/24

STATUS: Terminated

TITLE: True Negative Rate of Mammography as Confirmed by Biopsy

START DATE: Jun 90

ESTIMATED COMPLETION DATE: Jun 91

PRINCIPAL INVESTIGATOR: CPT John Haeberlin

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL John F. McPhail, III, MC; MAJ Stephen Carey, MC; CPT Anthony J. Canfield, LTC Henry Butler, MC

KEY WORDS: Mammography, Biopsy

Study Objective: Check how many nonpalpable breast lesions, thought to be benign by mammography, are actually benign pathologically.

Technical Approach: Inclusion criteria for subjects are: (1) nonpalpable breast lesion seen by mammography, (2) no calcifications, (3) lobulated lesion, or (4) lesions with a less-than-25% indistinct border. Preliminary data will be reviewed after 100 patients admitted to the study group. There will be only one study group. Any patient that has a mammogram which fulfills the admission criteria and is 18 years of age or older will be offered a biopsy as part of the study. Dr. Wolsard will be the screening physician deciding admission into the study based on his mammographic reading.

Patients with coagulopathies will have necessary clotting, to include all or part of the following: P.T., PTT, CBC, thrombin time and/or bleeding time, studies besides being counseled on additional risks of the biopsy. A subject's participation will be terminated either when a negative biopsy report and proper wound healing is achieved or after patient has proper surgical therapy for a cancerous lesion.

One year is the expected duration, and the success criteria are truly negative lesions supported by a negative biopsy. Failure criteria are cancerous biopsies. The data will be collected and maintained by Dr. Haeberlin in both hard copy and computer disc. Mammographic data will be relayed by Dr. Wolsard. Pathology reports will be relayed by Dr. Nguyen.

The risk to the subject will be minimized by proper pre-operative evaluation for risks to excisional biopsy, preparation for biopsy and close follow-up after biopsy checking wound healing progress. The risk to benefit ratio is believed to be low. The major risks of biopsy to include infection and bleeding are easily averted with good surgical technique. The benefits include finding new criteria for evaluating mammography as a screening tool. Instead of repeating mammography with suspected benign lesions at six month intervals, this study may provide further assurance that lesions are truly benign thus making repeat mammography unnecessary. This can only help lower the cost of medicine.

Progress: The principal investigator was unable to begin this project due to insufficient time and decided to terminate.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/40

STATUS: Terminated

TITLE: Determination of Intrinsic Compartment Pressures in the Hand in Patients with Metacarpal Fractures
(Medical Monitor: COL Scully)

START DATE: Apr 90

ESTIMATED COMPLETION DATE: Jun 91

PRINCIPAL INVESTIGATOR: CPT Eric Hirsch

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ Larry Donovan, MC; MAJ Monte Watson, MS

KEY WORDS: Intrinsic compartment pressures, metacarpal

Study Objective:

1. Establish normal intrinsic hand compartment pressures.
2. Determine the intrinsic compartment pressures in skeletally mature patients sustaining metacarpal fractures.
3. Obtain data regarding elevated compartment pressures by measuring those pressures with a compartment pressure monitor.
4. Identify those groups of patients at risk for intrinsic compartment syndrome of the hand (e.g., associated crush injury, multiple fractures, etc.).

Technical Approach: The first 50 patients age 18 years and older, presenting to the Orthopaedic Surgery Service with metacarpal fractures (closed or open), or to the Trauma Unit, and who are skeletally mature, will be evaluated. Upon obtaining an informed consent, the intrinsic compartment pressure monitor. Also, the compartment affected hand will be determined with a portable compartment pressure monitor. Also, the compartment pressures of the uninvolved hand will be evaluated with this monitor. If there are metacarpal fractures in both hands, then pressures will be measured in both hands as well. All patients included in the study will have their blood pressure measured. All compartment pressures will be performed by the evaluating orthopaedic resident or attending. A portable compression monitor allows for accurate, easily reproducible measurements. Historical information to be recorded includes the patients name, identification number, address, and phone number. Also, the date, time, mechanism of injury, and other injuries found will be recorded. A presumptive diagnosis of compartment syndrome is made based upon pain with passive stretching; this is done by passively abducting and adducting the fingers with the MP joints in full extension and the PIP joints in flexion. Also, the thumb is stretched in palmar abduction and radial abduction. The little finger is examined by passive extension and adduction. All patients are to have a distal neurovascular exam, with particular attention to any loss of two point and pin prick sensation. Fasciotomy will be done for patients with a compartment syndrome. Patient follow up in the Orthopaedic Clinic and the Occupational Therapy Clinic will record the neurovascular status. Additionally, the range of motion of each digit at the MP, PIP, and DIP joints will be recorded for both hands. Muscle strength will be graded for finger abduction and adduction, thumb adduction and extension, and little finger MP flexion and abduction. Data will be analyzed to determine the risk of compartment syndrome with isolated fractures, multiple fractures, and crush injuries.

Progress: Only 12 patients volunteered; no abnormalities noted in any of them. Project terminated due to PCS of investigator.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 88/64

STATUS: Ongoing

TITLE: Microvascular Anastomosis of the Rat Femoral Vessels

START DATE: Nov 88

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: MAJ Jeffrey R. Keim

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Microvascular anastomosis

Study Objective: To gain proficiency in microvascular technique so that the technical proficiency gained can be applied to clinical conditions.

Technical Approach: Two survival femoral vessel anastomosis procedures and a third non-survival abdominal vessel surgical procedure will be conducted on each of 40 rats during the training year. At least one staff surgeon will supervise the resident training until they have become proficient. The first procedure (right femoral vessel anastomosis) will be conducted on day 0; the second (left femoral vessel anastomosis) on day 14; and the third (aortic artery anastomosis) will be conducted on day 28 for each respective rat. By the third training day, one of each of these procedures will be done every training period using 3 different rats. The rats will always be euthanatized immediately following completion of the abdominal procedure.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Fifteen animals were used. Several microvascular procedures have been performed for the benefit of teaching residents. Microvascular surgery is learned in the laboratory and not on the patient. This protocol has been invaluable in teaching the Plastic Surgery residents microsurgery. We need to continue the protocol for their benefit.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/61

STATUS: Ongoing

TITLE: Observations of a Pediatric Surgeon in the Persian Gulf War

START DATE: Aug 91

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: LTC Troy M. Reyna

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Pediatric trauma, Persian Gulf

Study Objective: To clearly and succinctly state the need for pediatric and pediatric surgery expertise in the military health care armamentarium of the United States military forces during an armed conflict such as the Persian Gulf War.

Technical Approach: A retrospective account of experience garnered in the recent Persian Gulf War will provide the design and substance of this study.

Progress: The 410th EVAC is a 400-bed med-surg deployable hospital. It was active in Saudi Arabia from 8 Feb 91 to 26 Apr 91. In that time 877 admissions were logged. Of the 877 admissions, 50 (5.7) were civilian pediatric. Forty of these children were admitted with trauma. The majority of injuries were secondary to cluster bombs. The deaths were not secondary to trauma, but to neglected medical disease, i.e., malnutrition/dehydration. Investigator working on paper which is 98% complete.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/11

STATUS: Ongoing

TITLE: General Surgery Department Vascular Surgery Training Program Utilizing the Porcine Model

START DATE: Jan 91

ESTIMATED COMPLETION DATE: Indef

PRINCIPAL INVESTIGATOR: LTC Lawrence Runke

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Vascular surgery training

Study Objective: This training is designed to teach General Surgery resident physicians the basic operative skills required to perform vascular surgery.

Technical Approach: The exercise will concentrate on developing the surgeon's ability and confidence in handling vascular tissues, sutures, and prosthetics. Survival and non-survival procedures will be performed on each animal.

(a) The first animal will undergo transection and primary re-anastomosis of the aorta and vena cava. It will be recovered for 7-14 days, then undergo placement of a peripheral (femoral) PTFE A-V fistula. The abdomen will be re-explored, and the original aortic and vena caval anastomosis will be examined. The animal will then be euthanatized while the animal is still under anesthesia.

(b) The second animal will undergo placement of an interposition Dacron sleeve graft of the aorta. It will be recovered, and in 7-14 days it will undergo formation of bilateral femoral Brescia fistulae. The abdomen will then be re-explored, and the aortic graft examined. The animal will then be euthanatized.

(c) The third animal will undergo placement of a peripheral (femoral) PTFE A-V fistula. It will then undergo laparotomy and formation of a portocaval shunt. It will then be euthanatized.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in Item 5.b. (Animal Procedures).

Progress: Although approved, training is not scheduled to begin until FY92.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/13

STATUS: Ongoing

TITLE: Resident Training in Laparoscopic and Open Stapling Techniques

START DATE: Mar 91

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: LTC Lawrence C. Runke

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Laparoscopic training

Study Objective: The objectives are to teach the surgical staff and residents proper thoracic and abdominal laparoscopic procedures utilizing stapling instruments and suturing techniques and proper open stapling techniques utilizing the multitude of gastrointestinal staplers, including the TA, GIA, EEA instrumentation, the LDS instrument and the Liga Clip Appliers.

Technical Approach: Both video laparoscope and open surgical training techniques will be conducted in the porcine model. The experimental design is such that one or both of the techniques will be conducted on each animal. When both laparoscopic and open techniques are utilized, the laparoscopic techniques will precede the open procedures. The determination of the techniques to be conducted will be done at the time of the training session and will be dependent upon the knowledge and expertise of the residents and staff being trained. After anesthesia induction, the following procedures will be conducted:

a. Video laparoscopic - Abdominal: Cholecystectomy, gastrectomy, small bowel resection, nephrectomy, hysterectomy, splenectomy and partial hepatectomy. Thoracic: esophagectomy, pulmonary resections and vagotomies will be performed utilizing the various stapling instruments and liga clips.

b. Laparotomy (Open) - Abdominal: A midline incision from the xiphoid process to the pubis will be made. Then a multitude of gastrointestinal staplers, including the TA, GIA, EEA instrumentation, the LDS instrument and the Liga Clip Appliers will be utilized to complete end-to-end, side-to-side colon and small intestinal anastomosis. Additionally, anastomosis will be completed between portions of the small intestine; from the small intestine to stomach and colon; and between the colon and rectum. Transection of the stomach, colon and small intestine will also be performed. Pulmonary: Transection of pulmonary tissue, bronchi, pulmonary arteries and veins will be performed utilizing the various instruments through an intercostal incision.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: To date, 8 porcine models have been utilized to train 8 residents.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 87/93

STATUS: Ongoing

TITLE: Prevention of Stress Fractures Through Modification of Basic Combat Training Physical Training Activities Based on Biodynamics

START DATE: Jul 89

ESTIMATED COMPLETION DATE: Jun 92

PRINCIPAL INVESTIGATOR: COL Thomas J. Scully

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL Roy W. Tate, MAJ Bruce H. Jones, MC, Janice E. Morales, RN/BioMedical Engineer

KEY WORDS: Stress fracture, Bone

Study Objective: To compare the incidence and distribution, over the course of basic training, of the occurrence of stress fractures, stress reactions, and other musculoskeletal injuries, among Army Basic Combat Trainees participating in one of four variations in physical training. The variations to be studied are (1) progressive training, (2) cycle training with avoidance of running and jumping during the second week, (3) cyclic training with avoidance of running and jumping during the third week and (4) reduced total running mileage.

Specifically, the purpose of this study is to determine whether avoidance of running and marching in the second or third week of training will reduce the incidence of stress fractures, stress reactions of bone and musculoskeletal injuries in general, when compared to progressive training. If there is a decrease in injury is specific to the response to cyclic training or rather due to the decreased running miles.

Technical Approach: The study will be conducted at USATC, Fort Bliss, Texas and WBAMC. 1200 basic combat trainees, 12 companies (80-100 per company) with 3 companies per study group. (Progressive, rest week 2, rest week 3, decreased training mileage.) Treatment groups will be assigned by random lot drawing at the beginning of each basic training cycle. Trainees' medical history will be followed through the completion of their individual AIT assignments. Each company will be studied in four phases.

PHASE 1: Preliminary measurements will be documented on each trainee from review of their physical entrance examination and their personal response to the questionnaires. Age, race, height, weight, flexibility of their feet, history of athletic activity, during the one month before start of basic training, history of past injury to lower limbs, and age of athletic shoes used prior to basic training will be obtained.

PHASE 2:

- a. Initial, intermediate, and final physical fitness test scores will be recorded on each trainee.
- b. The DI or Company commander will keep a daily training check list log to be picked up twice weekly at random times to insure logs are truly kept on a daily basis.
- c. All injuries and illnesses will be documented by screening of all medical records. All cases of lower limb pain will be treated according to the Stress Fracture Algorithm.
- d. All discharges (medical, EPTS, ELS) and recycles will be documented.

PHASE 3: Advanced Individual Training - 2nd follow-up period.

- a. Record initial and final PT test performance.
- b. Have commanders document unit level physical training in AIT with check list log.
- c. Follow medical records of subjects after BT through end of AIT for injuries and illness.
- d. Document administrative outcomes.

PHASE 4: Analysis.

- a. Univariate - Company vs. company chi square test of: fitness within each company, contrast injury experience of different quartiles of performance using partitioned chi squares.

b. Multivariate analysis:

(1) MH-CHI SQ stratified on age, race, and flexibility of foot, or same variables in a logistic regression model.

(2) Survival analysis conditional on age, race flexibility.

c. Debriefing Post HQ, TRADOC HQ, MRDC HQ.

Progress: ~~Progress:~~ In an attempt to define modifications of Army Basic Combat Training which would result in a reduction of the incidence of stress fractures of the bones of the lower limbs, we conducted an intensive study of 1,375 soldiers in six companies undergoing basic combat training at Fort Bliss, Texas.

Upon arrival at the reception station each soldier completed a questionnaire which provided historical data such as age, occupation, athletic experience, past injuries, education, and fitness preparation for BCT. Demographic data such as height, weight, % body fat, foot structure, flexibility, and diagnostic APFT scores were obtained for each soldier.

A daily, quantitative, physical fitness training log was maintained for each platoon in each training company throughout the training cycles.

Eighty-six soldiers reported on sick call with symptoms and signs of a stress reaction or stress fracture. These soldiers underwent a physical examination, routine roentgenograms, and thermographic studies. Bone scans were obtained on 79 of these soldiers. Follow up roentgenograms were also obtained. Of the 79 bone scans, one was normal, 12 showed grade I stress fractures, 25 grade II stress fractures, 17 grade III stress fractures and 24 grade IV stress fractures. Bone scans were not obtained on 7 soldiers who had frank stress fractures on routine roentgenograms upon initial evaluation. Forty-six of the 78 soldiers with positive bone scans had normal roentgenograms and eight had stress fractures confirmed by roentgenograms. Radiologic studies were not performed on the remaining 24 soldiers. Fortynine of the 78 soldiers with positive bone scans successfully completed basic training, including 11 with grade III scans and 15 with grade IV scans.

Bone scans were also obtained on 227 soldiers who had no symptoms of a stress reaction throughout training and who successfully completed training. These scans were obtained during the week of graduation from training. Only 4 had normal scans, 77 had grade I stress fractures, 95 had grade II stress fractures, 45 had grade III stress fractures and 9 had grade IV stress fractures.

Bone scans were obtained on an additional 39 soldiers when they reported to the reception station at Fort Bliss. Only 1 of these recruits had a normal bone scan. Four had grade I stress fractures, 29 grade II, 4 grade III and 1 a grade IV stress fracture. Bone scans were repeated on an of these trainees when they graduated from basic training. One scan was normal, 9 showed grade I stress fractures, 16 grade II stress fractures, 11 grade III stress fractures and 2 grade IV stress fractures. Of these soldiers, 18 had bone scans which did not change following basic training, 10 had scans which increased one grade in severity and 7 had scans which decreased one grade in severity.

Summary of Findings: These findings indicate that radiotracer bone scans provide little useful information for the evaluation of soldiers with suspected stress fractures or stress reactions of bone. Our data suggest that the majority of soldiers have at least grade II "stress fractures" when they report to reception stations prior to beginning basic training. Moreover, almost all soldiers have positive bone scans at the completion of basic training, even though they may be completely asymptomatic.

The diagnosis of a stress fracture must be based on confirmation of physical findings by routine roentgenograms, the "gold standard".

Only 15 of the 1375 soldiers in our study sustained stress fractures which were confirmed by roentgenograms. One soldier was in Company DIA, 2 in Company D3, 5 in Company E1, 4 in Company E3, 3 in Company C1 and 0 in Company D1B. Although different training methods were used in the various companies, it is difficult to state that any of the training modifications resulted in a reduction of the incidence of stress fractures because of the small number of fractures that were sustained. ^R

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 88/44

STATUS: Ongoing

TITLE: Determination of Bone Manganese Levels in Patients with Chondromalacia Patella. (Monitor: COL Maldonado)

START DATE: May 88

ESTIMATED COMPLETION DATE: Dec 92

PRINCIPAL INVESTIGATOR: COL Thomas J. Scully

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ John Cook, MC; MAJ John Uhorchak

KEY WORDS: Chondromalacia, Manganese

Study Objective:

1. Identify and characterize by symptoms and physical findings the patient group with patellofemoral pain syndrome.
2. When performing diagnostic arthroscopy of patients with knee impairments, observe and record the character of the patellofemoral articular cartilage including objective measurement of cartilage softness.
3. Obtain 1 gram bone biopsy specimens from the distal femoral metaphysis at the time of arthroscopy and determine manganese content of bone mineral.
4. Perform multivariate analysis of data to observe possible correlations of bone manganese levels with severity of signs and symptoms of chondromalacia, cartilage appearance and measure cartilage softness.

Technical Approach: The study will be conducted at WBAMC and UTEP. Clinical evaluation will take place at WBAMC. The patients presenting to the Orthopaedic Clinic with knee disorders requiring arthroscopy or arthrotomy will be counseled and asked to volunteer for this study. If their informed consent is obtained they will be asked to provide information to complete the clinical questionnaire. The results of a comprehensive physical examination of the knees will also be recorded. At arthroscopy or arthrotomy the character of the articular cartilage will be noted and graded for severity of chondromalacia by the criteria of Hugston, et al. The indentation hardness of the cartilage will then be measured by a modification of the Brinell hardness measurement technique. This will be done with a locally fabricated instrument which can be autoclave sterilized. A biopsy specimen consisting of 1 gram of bone will be obtained from the distal femoral metaphysis using standard bone biopsy techniques. A portion of the specimen will be submitted for routine histology and the remainder will be analyzed for manganese content. The portion for manganese assay will be asked at 900 degrees centigrade, the ash weighed, dissolved in EDTA decalcifying solution, and analyzed with a Beckman plasma spectrophotometer at UTEP. All biopsy specimens sent to UTEP will be identified by code number only.

Progress: All activity on this project was halted during Operation Desert Storm. No additional patients have been enrolled. The study will resume in February 1992.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/25

STATUS: Ongoing

TITLE: Vascular Changes Associated with Stress Reaction of Bone in the Rat

START DATE: May 89

ESTIMATED COMPLETION DATE: Jun 92

PRINCIPAL INVESTIGATOR: COL Thomas J. Scully

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: MAJ John M. Uhorchak, MC

KEY WORDS: Stress reaction, bone

Study Objective: To determine the sequence and character of vascular changes which occur in living bone after it has been subjected to repeated physical stress.

Technical Approach: We will study the character and chronological sequence of vascular changes which occur in rat legs subjected to mechanical stress in the absence of confounding electrical shocks.

a. Thirty anesthetized rats will have their left leg cyclicly mechanically stressed using the techniques of Scully et al. The tibias will be cyclicly strained to 0.5 mm by repeated application of a 3 point bending load. 10,000 cycles of strain will be applied to the left tibia of each rat at a rate of 10 Hz. The animals will then be recovered from anesthesia and maintained in standard laboratory cages with unrestricted activity, on a standard laboratory diet. Groups of 2 animals will be selected at random on days 0, 1, 2, 3, 4, 5, 6, 7, 10, 12, 15, 18, 24 and 30 days after the initial strain loading.

b. On the date selected the animals will be anesthetized with Nembutal at a dose of 25mg/kg Intravenously. The rats will then be heparinized and injected with Xylocaine to prevent vascular thrombosis and to ensure maximum vasodilation. The animals will then be given a lethal dose of Nembutal. After euthanasia the abdomens will be opened through a midline abdominal incision. The aorta and inferior vena cava will be transected and cannulated. Using techniques prescribed in the Microfil product literature the aorta and both lower extremities will be perfused with Microfil at a pressure of 150 mm of mercury. Perfusion will continue until the flow of the Microfil is returned via the inferior vena cava. At that point the animals will be refrigerated to allow overnight curing of the Microfil. As each animal has had only one leg stressed, the contralateral leg will serve as a control. Radiographs will be taken of both lower extremities to delineate the microvascular structure. Microfil is a radio-opaque material. After the radiographs are obtained, tissue clearing will be performed by the following technique: on the first day both tibias will be immersed in a 25% ethanol solution. On the second day 50% ethanol, on the third 75% ethanol, on the fourth day 95% ethanol and on the fifth day a new solution of absolute alcohol. On the sixth day the specimen will be immersed for 24 hours in methylsalicylate. If the tissue is not clear it will be returned to a 95 % ethanol solution and the fine cleaning procedure steps will be repeated. Photographs will then be taken of the vascular tree which will have been filled with colored Microfil. The tibias will then be imbedded and sectioned for standard histologic sectioning.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: All activity was halted during Operation Desert Storm and has only recently been resumed. Specimens have been preserved and are undergoing additional study.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/07

STATUS: Ongoing

TITLE: The Timing Principle: A comparison of vecuronium versus atracurium for rapid sequence induction of anesthesia

START DATE: Jan 91

ESTIMATED COMPLETION DATE: Apr 92

PRINCIPAL INVESTIGATOR: MAJ Sanford Silverman

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC S. Ciresi; MAJ C. Hauser; CPT V. Cassani

KEY WORDS: Vecuronium, Atracurium, Anesthesia

Study Objective: To compare intubating conditions with atracurium utilizing the timing principle.

Technical Approach: In an effort to define the effectiveness of these techniques, a prospective study will be undertaken to compare the timing technique to that of rapid sequence induction with succinylcholine. The study will utilize state-of-the-art monitoring and routine dosages of anesthetic agents. A comparison will be made as to whether atracurium is as reliable as vecuronium utilizing the timing technique.

Progress: Ten subjects have been studied so far: 3 in the control group, 3 in the atracurium group and 4 in the vecuronium group. No adverse sequelae or procedural problems noted. Study participation continues.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/66

STATUS: Ongoing

TITLE: Logistics of Surgery and Modern Warfare: Epidemiologic Review of the Lessons Learned in "Desert Storm" during Duty with a Combat Support Hospital

START DATE: Sep 91

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: MAJ William C. Sippo

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS:

KEY WORDS: Combat Support Hospital (ODS)

Study Objective: To define the modern military medical requirements for rapid mobilization , deployment, combat and aftermath of modern warfare with emphasis on improving future operations.

Technical Approach: Retrospective review of inpatient and outpatient records of patients treated during the operational period of the 18th Combat Support Hospital in Southwest Asia (Sep90-Mar 91).

Progress: Project just begun.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/82

STATUS: Ongoing

TITLE: Ultrasound Screening for AAA in Asymptomatic Males Over Age 55

START DATE: Sep 89

ESTIMATED COMPLETION DATE: Jul 92

PRINCIPAL INVESTIGATOR: CPT James B. Smith

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: COL John F. McPhall III, MC; CPT Donna Corvette, MC; MAJ Cass Conaway, MC; LTC James C. Griffith, MC

KEY WORDS: AAA, Ultrasound Screening

Study Objective: To ascertain the incidence of AAA (Abdominal Aortic Aneurysm) in asymptomatic males over age 55 admitted to WBAMC for other reasons.

Technical Approach: All males age 55 and older admitted to Internal Medicine or Department of Surgery wards at WBAMC will be included in the study (approximately 180 per month) and will receive an abdominal aortic ultrasound examination. Patients with prior abdominal aortic surgery for aneurysm or occlusive disease will be excluded. All participants will be provided with a written explanation of the protocol. Patients with known AAA previously proven by ultrasound or CT Scan need not be submitted to repeat examination, if last previous study was within the past 6 months. Patients will be notified of the results of the ultrasound examination. Patients with positive findings for AAA will be referred to Vascular Surgery Service for appropriate follow-up. A negative finding will result in completion of participation in the study. The study will run for six months.

Success/failure criteria: Aneurysm will be defined as enlargement of the anteroposterior or transverse aortic diameter more than 1.5 times the diameter of the proximal aorta, or greater than 4 centimeters in diameter.

Data Collection: Patients will be interviewed by a physician for pertinent history of smoking, HTN, CAD, ASPVD, hyperlipidemia, or family history of AAA (maternal versus paternal).

Ultrasound examination will be performed by the Department of Radiology using their standard real-time ultrasound equipment: Diasonics model DRF 400, and read by a staff radiologist.

Progress: Method of patient selection has been logistically cumbersome. Administratively, it would be more workable to solicit outpatients than inpatients due to concentration of patients being higher at one clinic, rather than soliciting cooperation of multiple hospital wards. PI will submit amendment for IRB consideration.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/12

STATUS: Ongoing

TITLE: Determination of Percutaneous Inoculum Size for Cannulated Needle, Suture Needle and Scalpel Using a Porcine Model

START DATE: Feb 91

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: CPT Walker A. Wynkoop

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Al Landry

KEY WORDS: Inoculum size determination

Study Objective: The purpose of this study is to quantitatively measure:

1. The percutaneous blood inoculum (PBI) size for cannulated needles, suture needles, and scalpels.
2. The relative blood inoculum size reduction by simple incision and debridement.
3. To use the above information to make recommendations for emergent active treatment of high risk inocula by type of injury.

Technical Approach: The study will be conducted in the Nuclear Medicine Service facilities at WBAMC. Frozen, unpreserved porcine cadaver feet harvested from euthanatized animals from other studies will be thawed to room temperature. Small amounts of investigator's blood will be mixed with technetium using standard nuclear pharmacy safety precautions in the WBAMC Nuclear Pharmacy. This facility is a federally licensed nuclear materials user; license # 42-05255-07. This blood will be used to create PBI by scalpel, suture needle, and cannulated needle. Inocula size will be measured before and after simple I+D.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Twenty feet have been collected from pigs which were euthanatized at the conclusion of other protocols. The feet were all used to determine inoculum size of simulated accidental sticks from needles and scalpels. The study shows that a cannulated needlestick with injection is 30 times larger; a scalpel injury is about equal to; and a suture needlestick is much smaller than the CDC standard cannulated needlestick. Debridement and irrigation show little reduction in the cannulated needle, suture needle and scalpel inoculum sizes, whereas, the cannulated needle with injection can be reduced by an amount equivalent to 10 cannulated needlesticks.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/16

STATUS: Ongoing

TITLE: Evaluation of Emergency Active Management of Accidental Exposure to Allogenic Whole Blood for Orthopedic Type Injuries in the Porcine Model

START DATE: Mar 91

ESTIMATED COMPLETION DATE: Jun 92

PRINCIPAL INVESTIGATOR: CPT Walker A. Wynkoop

DEPARTMENT: Surg

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: LTC Albert Moreno

KEY WORDS: Needlestick, HIV inoculum size

Study Objective: The purpose of this study is to evaluate:

1. The relative percutaneous blood-inoculum (PBI) size for cannulated needles, power driven smooth and threaded K-wires, and power driven twist drills.
2. The migratory behavior of the allogenic blood inoculum over time.
3. The efficacy of incision and debridement (I+D) in reducing the allogenic blood inoculum size.
4. The relative allogenic blood inoculum size reduction by I+D as a function time.
5. To use the above information to make recommendations for emergent active treatment of high risk inocula by type of injury, including a recommended time of efficacy.

Technical Approach: This study is to be an animal model study using juvenile porcine swine. One swine will model a "high risk" patient. It will have it's whole blood tagged with technetium. Another swine will model an "ortho staff" member of an orthopedic surgical team. This "ortho staff" swine will then be inoculated with allogenic blood from the "high risk" swine using protocols modeling an accidental percutaneous blood inoculation. The study will be conducted in five one-day sessions (with provision for a 6th make-up session). A total of 10 swine will be utilized. Each session will be limited to one type of accidental orthopedic percutaneous inoculation.

Sharp instruments in the orthopedic OR suite cause PBI in various ways. The most dangerous are those that carry a large whole blood inoculum. This study will look at several accidents that can happen during open reduction and internal fixation of bone fractures. Power tool use during palpation of a bone fragment is often the best way to fixate a bone without added soft tissue stripping. This method runs the risk of causing a PBI by a power tool that has just traversed soft tissue and bone.

In order to model these injuries *in vivo*, two swine under general anesthetic will participate as the "high risk patient" and the "ortho staff". Accident mechanisms to be study are phlebotomy needlestick held by syringe plunger; phlebotomy needlestick held by syringe body; power driven twist drill; power driver smooth K-wire; and power driven threaded K-wire. The following variables will be measured for each accidental mechanism: 1) The effect of time on inoculum size. Will the allogenic blood migrate from the injury site over time?; 2) The effect of immediate, limited I&D on inoculum size; 3) The effect of delayed, limited I&D on inoculum size. Nuclear scanning will be used for determination of inoculum size with counts time-adjusted for decay. Scans will be taken at each step of the procedure.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in item 5.b. (Animal Procedures).

Progress: Six animals were assigned: 3 to cannulated needle sticks, 1 as twist drill donor; 1 as twist drill recipient; and 1 as a whole blood donor for tagged cells. An abstract is in preparation based on outcome of this study and the in vivo needle stick inoculum study, WBAMC Protocol #91/12.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/74

STATUS: Ongoing

TITLE: Effectiveness of Splinting for Carpal Tunnel Syndrome During Pregnancy

START DATE: Nov 89

ESTIMATED COMPLETION DATE: Dec 91

PRINCIPAL INVESTIGATOR: CPT Robbie Courts

DEPARTMENT: OT

FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS:

KEY WORDS: Carpal tunnel syndrome, pregnancy, splinting

Study Objective: To determine if volar wrist splints are effective in decreasing subjective and objective symptoms of carpal tunnel syndrome during pregnancy.

Technical Application: Use of survey form to assess subjective and objective symptoms of CTS during pregnancy, to be measured over a period of time: (1) initial referral, (2) one week after splinting, (3) additional follow-up if no improvement of symptoms after one week of splinting, (4) four weeks postpartum to see if symptoms are absent without splinting (indicating full recovery), (5) additional follow-up or referral to orthopedics PRN if symptoms persist postpartum.

Treatment includes patient education on carpal tunnel syndrome and importance of wrist positioning during sleep and activities, fabrication of thermoplastic volar wrist splint(s), measurements of grip and pinch strength, sensation (sharp/dull and two-point), range of motion (if not within normal limits), and documentation of subjective symptoms. Nerve conduction studies will not be ordered due to expense, uncomfortableness of the test, and expected short duration of the CTS symptoms during pregnancy.

The subjects included in the study will consist of all pregnant women referred to OT with symptoms consistent with CTS.

OT staff will collect data on a survey form using patient interview and standard methods of testing for grip, pinch, sensation, Tinnel's and Phalen's.

Progress: As of Sep 91, data collection has been completed on 51 subjects; 11 other subjects are in various stages of data collection. Fifty-three patients were withdrawn from the study, primarily for not returning for follow-up appointments. It is questionable if symptoms improved to such an extent that subjects are not interested in making the effort to return for the follow-ups or if other factors may be involved. Phone call reminders have been initiated to increase compliance in this area. Efforts continued with TEXCOM to set up a computer program for data collection and statistical comparisons. Early data indicates a decrease in all subjective symptoms (except swelling) after one week of the splinting protocol and an increase in bilateral grip and pinch strength. At one month post-partum, 90% of patients are symptom-free; the remaining 10% are symptom-free by 10 weeks post-partum. Grip and pinch were still less than average (for age/sex) at one month post partum.

No new subjects will be enrolled after Dec 91. The study will be closed when data collection is completed on all enrolled subjects.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 88/77

STATUS: Terminated

TITLE: Use of Venous pH in the Initial Evaluation of Pediatric Patients with Diabetic Ketoacidosis

START DATE: Oct 88

ESTIMATED COMPLETION DATE: Oct 91

PRINCIPAL INVESTIGATOR: MAJ Daniel J. Dire

DEPARTMENT: ER

FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS:

KEY WORDS: Venous pH, diabetic ketoacidosis

Study Objective: To determine the utility of venous pH to define the degree of acidosis in the initial evaluation of the pediatric patient with diabetic ketoacidosis.

Technical Approach: We will compare an arterial and venous pH sample in all patients who present in diabetic ketoacidosis to the emergency room at Darnall Army Community Hospital over an 18-month period, or until a sufficient population size is reached (N=100). Patients will be eligible for this study if they are between the ages of 1 and 18 years old, and have clinical and laboratory evidence consistent with ketoacidosis or who are known diabetics who have presented with similar symptoms of ketoacidosis in the past. A single sample (1.5cc) of arterial blood will be obtained from the radial artery of the patient by an emergency room staff member or by the investigators, as is the standard for defining acidosis in this setting. A single sample (1.5cc) of venous blood will also be obtained simultaneously with the other venous samples taken from the IV once intravenous access has been established. These two values will be compared and the results analyzed statistically. Consent for the additional laboratory study will be obtained, although no additional sampling procedures will be necessary.

Demographic and laboratory data will be recorded on a database form initiated in the emergency room and subsequently entered into a computer for statistical analysis in collaboration with the Department of Clinical Investigation at William Beaumont Army Medical Center.

Progress: Previous PI (Dr. Callahan, Peds) moved without completing study.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/02

STATUS: Completed

TITLE: A Comparison of the Stimson and Hennepin Techniques in the Reduction of Anterior Shoulder Dislocation (Monitor: MAJ R. Wilkerson)

START DATE: Nov 88

ESTIMATED COMPLETION DATE: Dec 90

PRINCIPAL INVESTIGATOR: MAJ Daniel J. Dire

DEPARTMENT: ER

FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS:

KEY WORDS: Shoulder dislocation

Study Objective: To determine if there are significant differences between the Hennepin and Stimson techniques of shoulder reduction in regards to the time required for reduction, subjective patient appraisal of discomfort during reduction, and post-reduction complications.

Technical Approach: All patients who present to the Emergency Department with suspected anterior shoulder dislocations will be evaluated for participation in this study. Patients who meet the following conditions or circumstances will be excluded from participation: Pregnancy; allergic to neperidine or hydroxyzine; history of liver or renal dysfunction; head injury; altered mental status; presence of pre-reduction fracture; intoxication from drugs or alcohol; or prior administration of pain medication.

All patients will be examined radiographically, with standard scapular AP and lateral views to examine for pre-reduction fractures and the type of dislocation. A strict neurovascular examination will then be performed. After the completion of the above, an initial injection of Meperidine (1.5mg/kg) and Hydroxyzine HCl (8.5mg/kg) will be given intramuscularly. The patient will then be allowed to relax for 30 minutes. At that time, the patient will be randomized (by draw of random numbers) to one of two treatment groups.

Treatment Group 1: Patients within this treatment category will undergo attempted reduction of their dislocation by the technique previously described by Leidelmeier and Mirick, commonly referred to as the Hennepin maneuver. If the reduction is not successful, two additional attempts may be made with or without added analgesia or muscle relaxers. If reduction is unsuccessful after repeated attempts, the Stimson technique will be attempted once. Immediate referral to the Orthopedic Surgery Service will be made for those patients in whom reduction has not been achieved.

Treatment Group 2: Patients within this treatment category will undergo attempted reduction by the Stimson technique, as previously described. If unsuccessful after one attempt for 20 minutes, the Hennepin technique will be attempted once. Immediate referral to the Orthopedic Surgery Service will be made for those patients in whom reduction has not been achieved.

All attempted reductions of dislocated shoulders will be performed by one of four physicians, who shall standardize their technique prior to the study. All are experienced in the above methods of reduction.

After the completion of attempted reduction, radiographic survey will be made using the scapular AP, lateral and axillary views.

After post-reduction radiographs are taken, the patients in both groups will undergo immobilization. All patients will be re-examined for neurovascular integrity. All patients will then be referred to the Orthopedic Surgery Service, as usual, for follow-up care.

Patients who at any time during the study exhibit respiratory depression, hypotension, dystonic reactions, and/or significant discomfort will be withdrawn from the study and will be treated for these complications in the appropriate fashion.

Patients who exhibit a return to normal function, relief of pain, and a radiographically reduced glenohumeral joint will be deemed a success. Failure to meet the above criteria will be deemed a failure.

Data regarding the amount of analgesia, time required for reduction, subjective appraisal of the pain felt, and complications resulting from reduction will be collected for entry into a computer data base (see enclosed data form). This information will be analyzed by discriminant analysis or other method of multivariant analysis for statistical difference between the two groups and their inherent measurements. A t-test analysis will be used to ascertain matching between the groups in relation to age, sex, body build, time from injury to first attempt at reduction, and to completion of reduction.

Progress: There were 15 patients randomized to Group EXRO and 11 to Group HGWT. Data from one Group HGWT subject was eliminated (spontaneous reduction occurred prior to active intervention) leaving 10 subjects. Previous dislocations were reported in 8 Group EXRO and in 9 Group HGWT patients ($P = .217$). The mean age of each group was 23.6 and 23.5, respectively. The mean times from injury to initial IM medication, initial IM medication to first attempt at reduction, and initial attempt at reduction to successful reduction were 89.1 and 87.4 ($P = .909$), 31.1 and 35.3 ($P = .2504$), and 28.0 and 11.2 ($P = .0805$) minutes for both groups, respectively. Patients rated HGWT less painful than EXRO ($P = .0596$). Successful reduction was accomplished by the initial technique in 9/15 (60%) of Group EXRO and 9/10 (90%) of Group HGWT patients ($P = .179$). All patients not successfully reduced by the primary technique were reduced by one attempt of the alternate technique. All patients not reduced on the first attempt of EXRO eventually required HGWT. Additional medications were required in 7/15 (47%) of the EXRO and 2/10 (20%) of the HGWT patients ($P = .229$). Overall, EXRO resulted in successful reduction in 10/16 (63%) and HGWT in 15/16 (94%) patients ($P = .083$).

Conclusion: Patients randomized to have the HGWT technique attempted first showed a trend towards a shorter time until successful reduction, less pain during reduction, and greater success. Dislocations not reduced by one attempt at EXRO should have HGWT performed.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/87

STATUS: Completed

TITLE: A Prospective Evaluation of Topical Antibiotics in Preventing Infections in Uncomplicated Soft Tissue Laceration

START DATE: Oct 89

ESTIMATED COMPLETION DATE: Dec 90

PRINCIPAL INVESTIGATOR: MAJ Daniel J. Dire

DEPARTMENT: ER

FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: David A. Dwer, CPT, MC; Marco Copola, CPT, MC; Jerry Karr, CPT, MC; John J. Lorette, Jr., CPT, MC

KEY WORDS: Infections, Topical Antibiotics

Study Objective: To show whether there is a statistically significant difference in the infection rates among uncomplicated repaired lacerations that are dressed with topical Bacitracin, NeosporinR, SilvadeneR, or placebo.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Project completed and data reported on 426 patients. Among the groups, there were no significant differences in patient age; sex; wound location, type, length, and depth; time elapsed from injury to emergency department treatment; scrubbed or debrided wounds; amount of irrigant or anesthetic agent used; number of SW and cutaneous sutures used; and compliance with the topical agents given. The BAC group had 6 infections (5.5%); NED group had 5 infections (4.5%); SIL group had 12 infections (12.1%); and PTR group had 10 infections (17.6%) ($P = .0034$).

Conclusion: Bacitracin and Neosporin-R groups had significantly lower infection rates than Silvadene-R or placebo groups.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/02

STATUS: Ongoing

TITLE: A Prospective, Multicenter, Clinical Trial Comparing Single Dose Intravenous Ceftriaxone and Oral Amoxicillin for the Prevention of Wound Infection in Cat Bites (Monitor: LTC Falbey)

START DATE: Sep 90

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: MAJ Daniel J. Dire

DEPARTMENT: ER

FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS:

KEY WORDS: Cat bite

Study Objective: To study the effectiveness of three antibiotic regimens (ceftriaxone alone, amoxicillin alone, and ceftriaxone plus amoxicillin) in preventing infection after a cat bite.

Technical Approach: All patients who present to the ER with a cat bite, and satisfy the criteria for entry into the study, will be invited to participate in the study as per the guidelines set forth.

Those consenting to the study will be assigned to one of the three treatment groups based on a pre-determined schedule based on the date of presentation to the ER. The study is not blinded and no placebo will be used. All of the patients entered will receive antibiotic prophylactic.

All wounds, regardless of the group, entered will be cultured before wound care is begun using standard culture medium. Local wound care will include high pressure irrigation using a 20 cc syringe and a 18 gauge catheter with 500 to 1000 cc of normal saline and debridement of devitalized tissue, if needed. Wounds will be left open unless closure is deemed necessary for cosmesis. Topical antibiotics will not be used. The wounds will be covered with dry dressings. All patients will receive tetanus prophylaxis and rabies prophylaxis, if necessary, in accordance with existing ER protocols.

Group I patients will receive 1 gram ceftriaxone (50mg/kg in children <40 kg) intravenously in 50cc of normal saline over 30 minutes). Group II patients will receive amoxicillin 250mg orally (pills or suspension) 3 times a day for 5 days. Group III will receive both ceftriaxone and amoxicillin in the same dosages as for Groups I and II.

All of the patients will receive the first dose of antibiotics in the ER as soon as possible after their entry into the study and the wound culture has been obtained, but prior to any wound care.

All wounds will be re-examined at 24, 48, and 72 hours after being seen in the ER. Wound will be evaluated using a standardized graduated scale for evidence of erythema, swelling, tenderness, warmth, drainage, lymphangitic spread, lymphadenopathy, systemic symptoms, overall clinical impression, and disposition. Follow-up cultures will be obtained from any wound discharge, if present. A phone call to the patient 7 days after presentation to the ER will conclude our follow-up period.

Progress: Eighteen patients have been entered as follows: Group I - 7; Group II - 6; Group III - 5. No adverse outcomes occurred. All data was forwarded to the collaborating institution (Univ of MA) for analysis. No data has been analyzed yet.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/44

STATUS: Ongoing

TITLE: Comparison of Intramuscular Meperidine and Promethazine, with and without Chlorpromazine for Pediatric Sedation

START DATE: Sep 90

ESTIMATED COMPLETION DATE: Dec 91

PRINCIPAL INVESTIGATOR: MAJ Daniel J. Dire

DEPARTMENT: ER

FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: John J. Lorrette, MAJ, D.O.; Thomas E. Terndrup, M.D.

KEY WORDS: Pediatric sedation

Study Objective: To determine if there is a significant difference in the efficacy of sedation and frequency of moderate complications after intramuscular meperidine and promethazine, with and without chlorpromazine.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation, WBAMC, and are available upon request.

Progress: Enrollment is complete with 15 subjects participating from Darnall Army Community Hospital. Data on these subjects were sent to the collaborating institution (SUNY-Syracuse) where data analysis will be conducted during the next few months. A total of 87 patients were enrolled from all the participating emergency departments.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/57

STATUS: Ongoing

TITLE: A Double-Blinded Comparison of Diphenhydramine Versus Lidocaine as a Local Anesthetic

START DATE: Oct 90

ESTIMATED COMPLETION DATE: Oct 92

PRINCIPAL INVESTIGATOR: MAJ Daniel J. Dire

DEPARTMENT: ER

FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: MAJ David E. Hogan, MC

KEY WORDS: Anesthetic, Lidocaine, Diphenhydramine

Study Objective: To determine if there is a significant difference in the efficacy and side effects of 1% diphenhydramine versus 1% lidocaine as a local anesthetic.

Technical Approach: Twenty volunteers (residents or nursing personnel) will be recruited for this double-blinded study if they are over the age of 21, healthy by history, not on any prescription or over-the-counter medications, have not taken any antihistamines within the last week, are not pregnant by history, and are not allergic to lidocaine or diphenhydramine.

The pharmacy will randomly prepare coded syringes which will contain either 2 cc of 1% (20 mg) lidocaine or 2 cc of 1% (20 mg) diphenhydramine.

The volunteers mid-volar forearm will be cleaned with an alcohol pad and a 2.4 cm diameter circle will be drawn on it with a sterile skin marker. Baseline sedation levels and sensation to pinprick will be recorded by each patient using a visual analog scale. The 2 cc volume of study solution will then be injected into the skin (subcutaneously) inside of the circle utilizing a 27 ga needle. The determination of sensation to pinprick will be done using a separate sterile 18 ga needle for each volunteer with care taken not to penetrate the dermis. After a one week washout period, the volunteers will be asked to return, at which time the other study solution will be tested in the same manner on the volunteer's opposite forearm.

The emergency department is equipped with all the equipment and medications and the investigators are residency trained, board certified or board prepared, emergentologists trained to treat any allergic reactions that might be encountered in the subjects.

Progress: Study will begin when 10 volunteers are recruited.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/17

STATUS: Terminated

TITLE: The Incidence of Abnormal Electrocardiograms in Emergency Department Patients with Head Trauma

START DATE: Mar 89

ESTIMATED COMPLETION DATE: Jul 91

PRINCIPAL INVESTIGATOR: CPT David E. Hogan

DEPARTMENT: ER

FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: CPT Daniel J. Dire, MC

KEY WORDS: Electrocardiograms, Head trauma

Study Objective: To show whether there is a significant incidence of electrocardiographic (EKG) abnormalities, especially dysrhythmias, in Emergency Department (ED) patients with head trauma.

Technical Approach: All patients who present to the ED for initial treatment of any head injury (e.g., blunt trauma from falls, assaults, or vehicular accidents and penetrating trauma such as gunshot wounds or open skull fractures) will be evaluated for participation in this study. Informed consent will be obtained from all patients except those with an altered mental status.

Patients will be excluded from this study if they have any of the following: History of chest pain, cardiac disease, prior abnormal electrocardiograms, or a history of prior dysrhythmias; history of seizure disorders or patients who are actively seizing; patients on any of the following type of drugs: anticholinergics, antihistamines, antidysrhythmics, antileptics, beta blockers, calcium channel blockers, decongestants, theophyllines, sympathomimetics (including cocaine and amphetamines); less than 16 years old; major blunt or penetrating chest trauma with signs or symptoms of myocardial injury, pulmonary contusions, or hypoxia; or patients in circulatory shock.

Cardiac monitoring will be initiated on all patients upon their presentation for treatment to the ED and will continue for a minimum of one hour. A 12-lead EKG will be performed during the course of their treatment.

A healthy, non-traumatized, age/sex matched control will be solicited from the ED waiting room who must not have any of the exclusion criteria listed above. Also, they must not be a patient waiting to be seen. Informed consent will be obtained from these subjects, a 12-lead EKG will be taken, and cardiac monitoring will be initiated for 1 hour.

Epidemiological and clinical data will be collected at the time of initial presentation.

All EKG's will be read by a staff internist who will be blinded to its source. The EKG interpretations will be recorded. Data will be entered into a computer database and analyzed in collaboration with the Department of Clinical Investigation, WBAMC.

Progress: Study terminated. PI deployed.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/16

STATUS: Ongoing

TITLE: An Evaluation of Clinical Criteria for Predicting Serious Bacterial Infections in Febrile Infants Two Months of Age or Less

START DATE: Mar 90

ESTIMATED COMPLETION DATE: Mar 92

PRINCIPAL INVESTIGATOR: CPT Kenneth D. Locke

DEPARTMENT: ER

FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: Charles W. Callahan, Jr., CPT, MC; Daniel J. Dire, CPT, MC

KEY WORDS: Febrile infants

Study Objective:

1. To test the predictive value of a predetermined set of clinical and laboratory findings along with subjective "impression of sepsis" for predicting serious bacterial illness in febrile infants two months of age or less in a community hospital emergency department.
2. To compare the use of these criteria and the subjective impression of three groups of physicians: emergency medicine residents, emergency medicine staff physicians, and staff pediatricians.

Technical Approach: This will be an observation study only. All of the diagnostic tests performed are those tests that we routinely perform in the evaluation of a febrile infant less than or equal to 8 weeks old (except the C-Reactive Protein which will not require any additional blood to be drawn).

All febrile (T >100.3 R) infants 8 weeks of age or less who present to the emergency department of Darnall Army Community Hospital will be eligible for the study. Patients will be excluded if they have had a previous hospitalization or were delivered prematurely. Patients will be evaluated and treated according to the usual practices employed in the setting where the infant is seen. This will include a physical examination; laboratory tests to include a complete blood count, SMA 7, urinalysis, urine culture and Welcogens, blood culture (1 set), erythrocyte sedimentation rate, C-reactive protein titer, and a stool culture (if indicated based upon the history); chest X-ray; and CSF will be obtained for cell counts, protein, glucose, gram stain, culture and Welcogens. An intravenous line with D5W in 0.25 NS is usually established during venipuncture for laboratory specimens. No changes in the management of these patients will be necessary. No new interventions will be made in the care of these patients as a result of their inclusion into this protocol.

Serious bacterial illness will be defined as bacteremia, meningitis, cellulitis, osteomyelitis, bacterial pneumonia, bacterial gastroenteritis or colitis, or urinary tract infections. Patients will be considered to be high risk for serious bacterial illness if they have any one of the following predictor variables: Strong clinical impression of sepsis based on the general appearance of the patient, irritability, consolability, the presence or absence of a social smile, and subjective assessment of "toxicity" by the examining physician; total white blood cell count less than 5,000/mm³ or greater than 15,000/mm³; absolute band neutrophil greater than 1,500/mm³; urinalysis with 10 or more white cells per high power field in a spun specimen or the presence of any WBC's or bacteria on an unspun specimen; stool with 25 or more white cells per high power field in a child with diarrhea; erythrocyte sedimentation rate greater than or equal to 55% by the Zetafuge Sedimentation Rate (Coulter Electronics); positive C-Reactive Protein; or the presence of neutrophilic vacuolization or toxic granulations on the peripheral smear.

Patients who do not have one or more of these predictor variables will be considered to be low risk for serious bacterial illness. The clinical impression of sepsis by the emergency resident, emergency staff, and pediatric staff will be recorded along with the laboratory values.

The investigators will examine all of the patients' peripheral smears to evaluate for the presence or absence of neutrophilic vacuolization or toxic granulations.

The Staff Pediatrician on call will be consulted to evaluate every patient for hospitalization and antibiotic therapy. Outcome variables will include the standard definitions for each of the serious bacterial illnesses noted above; for example, bacteremia defined as a positive blood culture for a pathogenic organism within 72 hours of admission.

Progress: Twenty subjects were entered in the protocol. Project has been delayed due to Desert Storm deployment.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/22

STATUS: Terminated

TITLE: A Simple Approach to Scalp Laceration Repair

START DATE: Sep 90

ESTIMATED COMPLETION DATE: Jun 91

PRINCIPAL INVESTIGATOR: MAJ John T. McDonnold

DEPARTMENT: ER

FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: James Alan Morgan, MAJ, MC; Donald M. Yealy, CPT, MC

KEY WORDS: Scalp laceration repair

Study Objective: To compare the wound infection complication rates of simple scalp lacerations that have been sutured with and without prior hair shaving.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation, WBAMC, and are available upon request.

Progress: Terminated due to insufficient number of volunteers.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/19

STATUS: Ongoing

TITLE: Effect of Multidose Activated Charcoal on Ethanol Elimination

START DATE: Mar 90

ESTIMATED COMPLETION DATE: Oct 91

PRINCIPAL INVESTIGATOR: CPT Ronald Moscati

DEPARTMENT: ER

FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: Paul Vinsel, CPT, MC; Donald Yealy, CPT, MC

KEY WORDS: Multidose charcoal, Ethanol

Study Objective: Demonstrate whether multidose charcoal can enhance the elimination of ethanol in humans.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: Protocol was delayed due to Desert Storm deployment. Subjects are being recruited and enrolled with no deviations from the original protocol.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/18

STATUS: Ongoing

TITLE: Evaluation of Partial Hospitalization Program

START DATE: Apr 91

ESTIMATED COMPLETION DATE: Jan 93

PRINCIPAL INVESTIGATOR: CPT J. Thomas Pichot

DEPARTMENT: Psych

FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: Dr. M. David Rudd

KEY WORDS: Suicide, Day treatment, Prevention

Study Objective: Given that the proposed project is an initial effort to implement a structured and replicable day hospital program for young adults identified as being at high risk for future suicidal behavior, the program has both identifiable short and long-term goals.

Short-term objectives of the proposed program include: 1) Implement and modify as indicated by ongoing evaluation, a structured and replicable short-term, intensive secondary prevention program for young adults identified as being at high risk for suicide or suicidal behavior; 2) Develop a detailed, standardized manual for the design, implementation, operation, and evaluation of the program. The manual will be comprehensive, covering the content and procedures for all program components. This will allow for generalization of the program outside its initial development site; 3) Experimentally test both the short and long-term safety and effectiveness of the program, focusing on both direct and indirect treatment effects. Given that the program is targeting suicide and suicidal behaviors as the primary treatment outcome, direct treatment effects include a reduction in the frequency and severity of reported suicidal ideation and related suicidal behaviors (gestures and attempts). Indirect treatment effects include a reduction in reported acute symptomatology, psychological distress, general psycho-pathology, and identified cognitive mediators such as hopelessness and general problem-solving skills (cognitive rigidity), with corresponding improvements in social/occupational functioning; 4) Monitor the program to ensure fidelity of both the treatment process (i.e., delivery of services in accordance with the structured protocol) and data collection; 5) Perform a cost-benefit analysis, comparing total treatment and associated costs (e.g., emergency room presentations, follow-up treatment costs, brief hospitalization costs, etc.) for a 1-year period for both the treatment and comparison groups.

Long-term objectives include: 1) Expansion of the program, to include implementation with the Fort Hood Department of Psychiatry Child and Adolescent Service (CAS). The goal is to expand the program to access the large clinical population currently seeking treatment through the CAS. Such an expansion would target local family members, 15-18 years old, identified as being at high risk for suicidal behavior; 2) Expansion of the program into the local community, coordinating with local school districts to identify patients and initiate local programs; 3) Replication at other sites, both inside and outside of the military.

Technical Approach: We shall use a rigorous pre-test/post-test control group design with follow-up at 3, 6, 12, 18, and 24 months. Patients who meet the inclusion criteria and are willing and able to participate in the experiment will be assigned randomly to either the proposed treatment program or the control group, traditional hospitalization (i.e., milieu therapy) or other outpatient treatment options. Patients who meet the inclusion criteria may not participate in the experiment either because they refuse to participate or because their commanding officer does not allow them to participate. Nonparticipants will be excluded from participation in the experiment at a later date if their suicidal ideation or behavior recurs. We anticipate that the nonparticipant rate will be less than 20 percent, based on personal observation of the principal investigators. Participants assigned to either treatment group may not complete the treatment plan and extended follow-up for a variety of reasons such as worsening condition (or death), unrelated medical problems,

or discharge from the service and subsequent refusal to participate. We anticipate that less than 20 percent of participants will be lost to such "censoring," based on personal observation of the principal investigator. Thus, all patients who meet the inclusion criteria will be classified either as Nonparticipants or Participants. In accordance with available DOP statistics, patients meeting the inclusion criteria will most likely be White males in their late teens or early twenties with a high school education. More specifically, 77% of DOP presentations are male, 23% female. With respect to race, 64% are White, 28% Black, and smaller percentages of Hispanics and Orientals. Approximately half (49.7%) of those presenting are married.

Progress: MAJ Pichot assumed PI responsibility. Dr. Rudd left the service, is full-time faculty with Texas A&M University, Health Science Center, and will continue to serve as co-investigator and project director. To date, four treatment cycles have been completed involving a total of 50 individuals. The first three cycles involving 31 individuals were deemed experimental in nature to facilitate and refine staff training, subject random assignment procedure, data collection/management, and general operational procedures for the intervention. Additionally, these initial trial cycles allowed staff to address issues of treatment fidelity, modify specific components of the treatment program, monitor subject recruitment and retention, and develop a workable schedule for treatment rotations and subject assessments. Although data was collected for these 31 individuals, it will not be integrated into the primary data base due to the experimental nature of the cycles. In addition to the fourth treatment cycle (N-19; 13 treatment, 6 control), 3-4 cycles will be completed by the end of the first year budget (Sep 91) with an estimated 82-103 participants (55-69 treatment and 27-34 controls). There have been no critical incidents with respect to self-destructive behaviors exhibited by participants. No particular problems have arisen with respect to recruitment or retention. Overall referrals and Department of Psychiatry patient load has been somewhat lower than prior to Desert Storm, and not all those eligible have agreed to participate. The project has developed an adequate referral base which appears, for the most part, consistent with projected numbers in the initial proposal.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/36

STATUS: Terminated

TITLE: A Multicenter, Randomized, Double-Blinded Placebo-Controlled Comparison of Paroxetine and Fluoxetine in the Treatment of Major Depressive Disorder (Monitor: MAJ David Orman)

START DATE: Jul 91

ESTIMATED COMPLETION DATE: Nov 91

PRINCIPAL INVESTIGATOR: CPT J. Thomas Pichot

DEPARTMENT: Psych

FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: Dr. Paul Hicks, CPT David Rudd, CPT Charles Engel, MAJ Thomas Hardaway, MAJ Richard Moczygemba

KEY WORDS: Major Depressive Disorder, Paroxetine, Fluoxetine

Study Objective: To compare the safety and efficacy of paroxetine to placebo and fluoxetine in the treatment of patients with Major Depressive Disorder.

Technical Approach: A total of 600 subjects for the full multicenter study will participate in the protocol. There will be 100 patients randomized to placebo, 250 patients randomized to paroxetine, and 250 patients randomized to fluoxetine. The Texas A&M College of Medicine/Darnall Army Community Hospital research center will enroll 30 of the total of 600 subjects for the multicenter study. Coded medication will be issued at the baseline visit, and each patient will be instructed to take his/her medication as outlined in Section 4.2 (page 11) of the SmithKline Beecham Paroxetine Protocol. Both active drug groups will begin treatment using a dosage of 20mg daily. The dosage may be increased if the therapeutic response is inadequate. For paroxetine, the increase will be by 10mg increments to a possible maximum dosage of 50mg daily. For fluoxetine, the dosage will be elevated by increments of 20mg to a possible maximum dosage of 80mg daily. Dose increases must be separated by an interval of at least seven days. Dosage may be decreased at any time during the trial if adverse events occur, or as deemed necessary by the investigator. The patient will be instructed to contact the investigator immediately should adverse events occur between visits.

Progress: Prior to enrollment of any subjects at Fort Hood, SmithKline Beecham notified the PI they were suspending all further enrollment of subjects into the multicenter study. The specific reason was not communicated, however, was reported as unrelated to development of the Ft. Hood protocol.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/29

STATUS: Ongoing

TITLE: Certification Training: Advanced General Surgery Laparoscopic Procedures in the Porcine Model

START DATE: Apr 91

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: COL Ramon Quinones

DEPARTMENT: Surg

FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: LTC Charles W. Van Way

KEY WORDS: Laparoscopic procedures

Study Objective: To provide training and certification of general surgery surgeons in laparoscopic cholecystectomy, hernia repair, and appendectomy. This training will enable them to develop the proficiency required to perform these operative procedures in human patients.

Technical Approach: No surgical procedures will be conducted without the administration of general anesthesia. Anesthesia will be administered and monitored by Dr. Schmurr and Dr. Mixon and animal care specialists. The animal's food will be withheld for a period of 18 hours prior to surgery. The pigs' hair will be clipped from the abdomen. The animals will be placed in dorsal recumbency. After the skin is prepped, an insufflation needle will be inserted and the abdomen will be filled and maintained with 15mm Hg pressure of CO₂. A trocar/cannula will be placed near the umbilicus for introduction of the video laparoscope which will enable monitoring of the procedure on a video screen. Two to three additional trocars/cannulas will be placed for introduction of laparoscopic graspers, scissors, laser fibers, etc. The cystic duct and artery will be bluntly dissected free, double ligated or clipped, and transected. The gallbladder will be dissected free from the liver bed by sharp, blunt, electrosurgical and laser techniques. Once free from hepatic parenchyma, the gallbladder will be approximated to the body wall, decompressed and pulled through one of the central trocar puncture sites.

Other advanced laparoscopic procedures will include hernia repair and appendectomy. Laparoscopic cannulas will be repositioned as necessary for subsequent procedures to enable visualization and tissue manipulation. Hernia repair: A defect will be created in the internal inguinal ring by sharp and blunt technique. Subsequently, the created hernia will be repaired by laparoscopic suture and stapling techniques. Appendectomy: The distal cecum will be isolated and mobilized. The distal segment will then be resected and closed by laparoscopic suture and stapling techniques. The appendage will be approximated to the body wall with large graspers and removed through a central puncture site.

NOTE: All procedures producing pain or discomfort to these animals have been described in full and such pain and discomfort will be effectively minimized with tranquilizers, and/or anesthetics as required under Public Laws 89-544, 91-579, 94-279, and 99-198 (The Animal Welfare Act and Amendments). All exceptions are described in the protocol in Item 5.b. (Animal Procedures).

Progress: Six surgeons (including 2 Gen Surg residents), 3 nurses and 4 technicians were trained. Twelve cholecystectomies were performed on 12 pigs with excellent results. The surgeons are currently performing laparoscopic cholecystectomies with minimal/no complications and the average OR time is 60-90 minutes. All are performing and training others with no difficulties. The program strength is mostly due to the course's hands on experience which is unequalled by courses available in the civilian community.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 91/32

STATUS: Ongoing

TITLE: An Investigation of the Incidence of Post Spinal Headache in Those Patients Who Flex and Elevate Their Legs and Hips Versus Those Who Remain Supine

START DATE: Jun 91

ESTIMATED COMPLETION DATE: Undetermined

PRINCIPAL INVESTIGATOR: CPT Richard Redgate

DEPARTMENT: Nsg

FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: CPT Robert Dominguez

KEY WORDS: Post spinal headache

Study Objective: To determine whether post subarachnoid block patients in the Post Anesthesia Care Unit (PACU), who flex their lower extremities and elevate their pelvis versus those who remain in the supine position and are discharged from the PACU using the sensory stimulation method experience a decreased incidence of post dural puncture headache (PDPH).

Technical Approach: Upon completion of surgery, all subjects will be transferred to the recovery room. While in the recovery room, Group I (experimental) subjects will remain supine and be discharged using the sensory stimulation method. Group II (control) subjects will follow the routine standard protocol currently in practice. Current protocol for discharge is ability to flex the lower extremities and elevation of the pelvis off the bed for 5-10 seconds. Group II subjects will be encouraged to flex/elevate their legs/hips every 15 minutes until discharged to the parent unit. Once on the ward, both groups will remain supine for 4 hours and then be allowed to resume activity as tolerated. At 24 hours postoperatively, subjects in both groups will be visited by one of the investigators (excluding the investigator who performed the actual spinal). Subjects will also be interviewed 48 hours postop in person if still an inpatient or telephonically if they have been discharged from the hospital. Because data generated by this study is the frequency of post-spinal headaches in two different treatment groups, the Chi Square test will be performed.

Progress: To date, PI unable to obtain necessary patient enrollment to provide study validity. Enrollment efforts continue.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 90/25

STATUS: Terminated

TITLE: The Effect of Visual Imagery as an Adjunct Therapy to Narcotic Analgesia in the Perioperative Period

START DATE: Apr 90

ESTIMATED COMPLETION DATE: Nov 90

PRINCIPAL INVESTIGATOR: 1LT Maureen Reilly

DEPARTMENT: Nsg

FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS:

KEY WORDS: Visual Imagery, Pain

Study Objective: To examine visual imagery as an effective adjunct therapy to narcotic analgesia in the male perioperative client undergoing lower limb surgery.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation, WBAMC, and are available upon request.

Progress: Study terminated. PI left service.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/47

STATUS: Terminated

TITLE: CSCC Program Evaluation

START DATE: Jun 89

ESTIMATED COMPLETION DATE: Sep 91

PRINCIPAL INVESTIGATOR: CPT M. David Rudd, PhD

DEPARTMENT: Psych

FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS:

KEY WORDS: CSCC

Study Objective: This project is designed to determine the relative therapeutic effectiveness of the CSCC program.

Technical Approach: All subjects will be active duty soldiers treated at Ft. Hood's CMHS. Participation is strictly voluntary. There will be 50 subjects from the CSCC program and 50 matched control subjects from other modalities of outpatient treatment. All subjects will be selected from cases dispositioned at the CMHS. The controls will be matched within five days of their initial CMHS sign-in, and will be matched to the CSCC subjects for demographic as well as selected clinical criteria, e.g., type of problem, severity.

This project uses a quasi-experimental approach with a pre-test/post-test design. The project design also includes follow up evaluations at one and three month intervals. Data collection involves the use of three standardized psychometric instruments (labeled the basic battery) and four instruments of local design addressing the subject's military performance. Of the locally designed instruments, two are intended for use as phone questionnaires which are to be answered by the subject's first line supervisor regarding performance of the subject within his unit.

Once a subject agrees to participate in the study, he will be given a pre-test consisting of the basic battery and the subject's self evaluation questionnaire. A research assistant will ensure completion of the first line supervisor's pre-evaluation. The post-test will be given after three weeks. It will consist of the basic battery and subject post-evaluation. At both the one month and three month follow-up evaluations, the subject will retake the basic battery and the post self-evaluation. A research assistant will complete post evaluations from first line supervisors at both of the follow-ups. The data collected will be analyzed using a completely randomized block design.

Any of the following will result in premature termination of a subject as a part of the study: failure to complete CSCC, subject refusal to continue participation in the project, ETS or PCS. Otherwise, subject's participation will be terminated after the completion of the three-month follow-up evaluation.

Progress: Protocol terminated due to staff shortages; no data collected.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #. 88/66

STATUS: Terminated

TITLE: Treatment of Hypercholesterolemia with Psyllium Hydrophilic Mucilloid (Metamucil)

START DATE: May 88

ESTIMATED COMPLETION DATE: Oct 90

PRINCIPAL INVESTIGATOR: CPT Richard E. Whitlow

DEPARTMENT: ER

FACILITY: Darnall Army Community Hospital

ASSOCIATED INVESTIGATORS: Julia A. Morgan, D.O.; Richard D. Harwood, R.N.P.; Rebecca J. Oskey, R.N.P.; Elizabeth Kist, R.D.; Ann Andersen, R.D.

KEY WORDS: Hypercholesterolemia, Psyllium Hydrophilic Mucilloid (Metamucil)

Study Objective: To define the optimal safe dosing of psyllium hydrophilic mucilloid to lower total and LDL cholesterol and define the long-term efficacy and safety of psyllium hydrophilic mucilloid. This study will be conducted in a randomized prospective, controlled manner.

Technical Approach: Patients will be enrolled from a variety of sources: random cholesterol screening tests, over-40 physical examinations, commanders' physical examination, commanders' total fitness course, and patients referred to Nutrition Clinic for dietary therapy. The patients will initially undergo a battery of screening tests as well as a history and physical exam to determine secondary causes of hypercholesterolemia (untreated hypothyroidism, obstructive liver disease, nephrotic syndrome). The study medication is psyllium hydrophilic mucilloid (blond Plantago psyllium, Metamucil) in varying doses and intervals. Only patients with serum cholesterols between 200 and 260 mg/dl with two coronary heart disease risk factors will be studied since therapy is recommended for this group by the NCEP and the magnitude of expected response is reasonable to assume a lowering of serum cholesterol by Metamucil to a normal range. Throughout the study, laboratory evaluations will be obtained to assess known aberrations induced by increased dietary fiber.

Progress: Project terminated. PI moved without finishing the project.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 88/52

STATUS: Ongoing

TITLE: Combat Trauma Life Support Procedure in the Sheep Model

START DATE: Oct 88

ESTIMATED COMPLETION DATE: Indefinite

PRINCIPAL INVESTIGATOR: CW2 Richard Harvey

DEPARTMENT: FBT

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: CW2 David Fisher, PA, WO1 Abelardo Montes, PA

KEY WORDS: Life support, Combat trauma

Study Objective: To train Physicians Assistants and Line Medics who are not dealing with major trauma on a day-to-day basis, but may be called upon to perform this function in a combat environment. The sheep model will simulate human trauma.

Technical Approach: Animal procedures include:

1. Cricothyroidotomy
2. Venous Cutdown
3. Intubation
4. Chest Trauma Management
 - a. Needle decompression
 - b. Tube thoracostomy

ATLS training manuals will be used for each training procedure.

Progress: Twelve field medics received training in one training session using two animals.

DETAIL SUMMARY SHEET

DATE: 1 October 90

PROTOCOL #: 89/42

STATUS: Ongoing

TITLE: The Utility of Thermographic Evaluation in the Diagnosis of Lower Extremity Injuries During Army Initial Entry Training

START DATE: Jul 89

ESTIMATED COMPLETION DATE: Sep 92

PRINCIPAL INVESTIGATOR: LTC Bruce H. Jones

DEPARTMENT: USAREM

FACILITY: William Beaumont Army Medical Center

ASSOCIATED INVESTIGATORS: Hamlet M., DVM; DiBenedetto M. (COL Ret)

KEY WORDS: Thermogram (graphic), Scintigraphic

Study Objective:

1. To document the sensitivity and specificity of thermography to detect the presence or absence of injuries in general compared to clinical standards and more specifically to:

(a) To document the specificity and sensitivity of thermography in the diagnosis of stress fractures verses bone scans and x-rays as the diagnostic standard. Also, to calculate the positive and negative predictive value of thermography in the diagnosis of stress fractures based on the prevalence of stress observed in this and other epidemiologic studies.

(b) To document the sensitivity and specificity of thermography to detect injuries other than stress fractures verses the level of certainty of clinical diagnosis, i.e., the presence or absence of observable signs and the number of positive signs such as swelling, erythema, ecchymosis, point tenderness, decreased range of motion, etc. for a particular diagnosis. Also, to document the sensitivity and specificity of thermography verses the degree of severity of injury measured in days of limited duty or hospitalization. Also, positive and negative predictive value will be assessed once the prevalence of specific injuries in the cohort are established. (As an aside, the potential for paradoxically decreased sensitivity of thermography when such soft clinical standards are used is recognized, however, the use of two or more operationally defined clinical standards, i.e., level of clinical certainty and degree of severity of the diagnosis should help to recognize a paradox when it arises.

2. To qualitatively and quantitatively describe the thermographic patterns for specific injuries if they are perceived to exist.

3. To determine whether the thermographic patterns "normalize" as injuries heal in a way that would assist in making decisions regarding return of soldiers to duty.

4. To determine whether individuals with flat feet or high arches are likely to suffer more injuries to the lower extremities than those with "normal" feet. Also, to determine whether the thermograms of individuals with flat feet or those with high arches are more likely to be positive (indicating "chronic stress") than individuals with "normal" feet at baseline (prior to onset of basic training) and episodically during basic training.

5. To determine the effect of training volume (running and marching mileage) on the incidence of injuries and on the qualitative and quantitative patterns of lower extremity thermograms.

6. To determine whether the thermographic patterns observed are more likely to be positive for sub-populations grouped on the basis of age, race, body composition, past activity, and physical fitness.

7. To determine the incidence of commonly occurring training-related injuries and the amount of morbidity (days of limited duty, etc.) associated with each. With these data estimates of the impact of early diagnosis and appropriate return to duty through use of thermography will be made.

Technical Approach: The details are lengthy and specified in the protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress: A total of 1374 subjects were enrolled. Data collection is complete. Data entry has also been finished and some preliminary analysis, as well. Preliminary quantitative analysis of the sensitivity and specificity of thermography versus bone scans suggests that thermography is not sensitive (25.6%, but is specific (93.3%). As an aside, however, it is difficult to know what to make of these results in light of COL Scully's recent study showing that bone scans are overly sensitive. Quantitative analysis of thermographic data by Dr. DiBenedetto is nearing completion.

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